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## URINARY INFECTIONS IN INFANCY AND CHILDHOOD

### DIAGNOSIS AND TREATMENT


HENRY F. HELMHOLZ, M.D.

ROCHESTER, MINN.


It is my purpose in this article to give in very concise form the essentials of diagnosis and treatment of urinary infections in infancy and childhood so that definite cure may be achieved in the simple forms of infection and relief obtained in the ones complicated by stasis or focal infection before irreparable injury of the kidneys occurs.

In the acute stage the urinary infections usually manifest themselves with symptoms of fever and pyuria, while in the chronic stage they may be found accidentally. Stasis in the urinary passage that is sufficient to cause marked reduction of renal function may be present for years without infection; therefore a primary infection may be associated with permanent injury of the kidney. When the patient is an infant or a child, fever that occurs without demonstrable cause is a clue to urinary infection, and examination of the urine establishes the diagnosis. The presence of pus in urine that is obtained in the usual uncontrolled way must be checked by catheterization if the patient is a girl, and if the patient is a boy a specimen of urine must be obtained after the prepuce and meatus have been cleansed. My experience has taught me that one should not start treating a patient for a urinary infection until one is certain that an infection is present in the urinary passages. If urinary infection is present it is important to know what type or types of bacteria are causing it. There are two procedures by which this information can be ascertained: (1) staining the sediment of the centrifuged urine with Gram's stain, and (2) a culture of the urine. By the former method it is possible to determine whether the infection is the result of gram-negative bacilli, cocci or a combination of the two. By means of cultures on eosin methylene blue agar one may differentiate the various gram-negative bacilli and Streptococcus faecalis, and by means of cultures on blood agar one may distinguish the other forms of cocci. The varied response of bacteria to different forms of treatment requires differentiation of infecting organisms.

The importance of normal renal function in the treatment of infections is best seen in the use of those methods of treatment that are dependent on a definite acidity of the urine. A defective kidney will not secrete a urine of sufficiently low $p_H$ or sufficiently high concentration of the drug to be bactericidal. This may apply to only a single kidney or to both kidneys. In cases in which mandelic acid therapy is used the normal kidney may excrete a urine which has a $p_H$ of 5.0 and contains 0.7 per cent of mandelic acid, and a kidney that is badly infected may excrete a urine that has a $p_H$ of only 6.0 and contains 0.2 per cent of mandelic acid; the former urine is strongly bactericidal but the latter is not bactericidal at all.

With the use of the ketogenic diet, mandelic acid and sulfanilamide, it has been possible to clear up urinary infections even in the presence of urinary stasis. Thus the inability to clear up urinary infection is no longer a reason for suspecting urinary stasis. It is essential, therefore, that an excretory urogram be made in all cases of urinary infection. This appears to be the only way in which it is possible to discover the presence of urinary stasis before the kidneys have been seriously injured.

The role of focal infection is difficult to evaluate. It is certain that foci of infection in the urethra and bladder may be responsible for the recurrence of infection and that removal of such foci may effect a permanent cure. When foci of infection occur in the ureters and kidneys, they can be removed only by surgical intervention. The relationship of distant infection, for instance infection of the tonsils, to urinary infection has been claimed by many physicians but it never has been proved to my satisfaction.

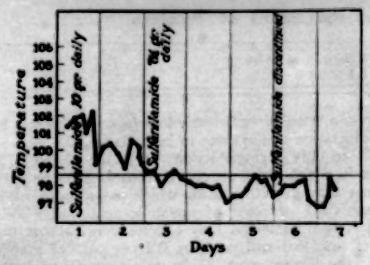
If the type of infection, the renal function and the presence or absence of urinary stasis are known, the special considerations which determine the choice of urinary antiseptic are important. The ease of administration of the drug, the concentration of the drug in the urine, the $p_H$ of the urine, the action of the drug on the various bacteria, the effect of lowered renal function and the possibility of toxic effects of the drug are the factors entering into consideration. It would seem that in a consideration of urinary antiseptics one has a wide choice, but in the last analysis two drugs stand out very prominently above the rest, namely mandelic acid and sulfanilamide.

Which of these two is the drug to use and why? Sulfanilamide has a number of very definite advantages over mandelic acid: it can be given in the acute stage of the infection, its bactericidal effect is not entirely dependent on reaction of the urine although it acts better in alkaline urine than it does in acid urine, and it is excreted in bactericidal quantities by kidneys that are so severely injured that the concentration of urea is from 75 to 100 mg. per hundred cubic centimeters of blood. The administration of sulfanilamide does not offer any special difficulties. It is taken readily by infants and older children by mouth, and when it is not


From the Section on Pediatrics, the Mayo Clinic.

Read before the Section on Pediatrics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

tolerated because of gastric irritability it can be given subcutaneously or intravenously. Its use in the acute stages of the infection, especially in infancy, is a definite advance over the previous use of only diuresis and alkalization. The chart shows a striking effect which was obtained in one case. The patient was a girl aged 8 months who had had a fever of 105 F. for a




Temperature during acute Escherichia coli infection in a case of pyelonephritis.

week. The kidneys were greatly enlarged; the left kidney extended to the level of the anterior superior spine of the ilium. Within forty-eight hours the temperature was normal; the kidneys decreased gradually in size and the child made an uneventful recovery.

In infections caused by Proteus ammoniae the urine is strongly alkaline. In the treatment of this type of infection sulfanilamide is the drug of choice because of its superior action in an alkaline urine and because of the difficulty in bringing the urine into the acid range necessary for bactericidal action with mandelic acid or methenamine. Table 1 shows the marked bactericidal effect on six strains of Proteus ammoniae and one strain of Proteus vulgaris. Table 2 shows the superior bactericidal action of alkaline urine at $p_H$ 7.5, as compared with the same urine at a $p_H$ of 6.2, on a variety of organisms. This and numerous similar experiments seem to indicate that the urine should be rendered alkaline when sulfanilamide is administered.

A particular advantage of sulfanilamide, which deserves great emphasis, is the possible concentration that is bactericidal in the urine of patients who have injured kidneys. It has been my experience with the ketogenic diet and with methenamine and mandelic acid that an injured kidney cannot secrete a urine of low $p_H$, and even in those cases in which the concentration of blood urea was normal the injured kidney could not be beneficially influenced because of this difficulty. It is, therefore, striking that sulfanilamide can be excreted in the urine in sufficient concentration in cases in which the concentration of blood urea is well above normal. It has been possible (table 3) to sterilize the urine in four of five cases; in one of these cases the ketogenic diet and mandelic acid were employed for many weeks but the urine did not become sterile. I also wish to emphasize that the urine did not remain sterile in all these four cases. In three of the four cases the urine remained sterile for some time after administration of the drug was discontinued. This has not been possible with any other urinary antiseptic.

These very definite advantages indicate why sulfanilamide is the most useful antiseptic in the treatment of ordinary urinary infections. There is just one serious handicap to sulfanilamide as the perfect urinary antiseptic, namely its complete failure in infection caused by Streptococcus faecalis. For some reason Streptococcus faecalis is resistant to the action of the drug and will grow luxuriantly in a urine that will kill Staphylococcus aureus, Escherichia coli, Aerobacter aerogenes, Proteus ammoniae, Pseudomonas and other gram-negative bacilli

TABLE 1.—*Bactericidal Effect on the Proteus Group of Urine Containing 51 Mg. per Hundred Cubic Centimeters of Free Sulfanilamide when Excreted*

| Strains of Proteus Ammoniae | Colonies in 0.5 Cc. of Urine: Before Incubation | Colonies in 0.5 Cc. of Urine: After 24 Hours |
|---|---|---|
| 1 | 1,020 | 110 |
| 2 | 1,500 | 0 |
| 3* | 110 | 0 |
| 4 | 320 | 0 |
| 5 | 4,300 | 0 |
| 6 | 6,000 | 240 |
| 7 | 720 | 0 |
| 8 | 480 | 0 |

* Proteus vulgaris.

TABLE 2.—*Bactericidal Action of 57 Mg. per Hundred Cubic Centimeters of Free Sulfanilamide Excreted in Urine at $p_H$ 6.2 and 7.5*

| Organism | $p_H$ 6.2 Colonies in 0.5 Cc. of Urine: Before* | $p_H$ 6.2 Colonies in 0.5 Cc. of Urine: After 24 Hours* | $p_H$ 7.5 Colonies in 0.5 Cc. of Urine: Before* | $p_H$ 7.5 Colonies in 0.5 Cc. of Urine: After 24 Hours* |
|---|---|---|---|---|
| Staphylococcus aureus | 770 | 330 | 230 | 0 |
| Escherichia coli | 670 | 3,600 | 600 | 0 |
| Aerobacter aerogenes | 30 | 4,000 | Innumerable | 28 |
| Proteus ammoniae | 700 | 4,000 | 700 | 0 |
| Pseudomonas | 2,400 | 7,500 | 5,500 | 1,700 |
| Streptococcus faecalis | ... | ... | 400 | Innumerable |

* Incubation.

TABLE 3.—*Use of Sulfanilamide in Sterilization of the Urine in the Presence of High Blood Urea*

| Case | Sex | Age, Years | Lesion | Blood Urea, Mg. per 100 Cc. | Organism | Dose of Sulfanilamide | Result |
|---|---|---|---|---|---|---|---|
| 1 | ♀ | 11 | Bilateral pyelonephritis | 84-180 | Escherichia coli | 5 grains 5 times a day* | Cure |
| 2 | ♀ | 11 | Chronic pyelonephritis | 232-300 | Escherichia coli | 5 grains 4 times a day | Failure |
| 3 | ♀ | 10 | Chronic pyelonephritis | 68-104 | Escherichia coli | 5 grains 5 times a day* | Sterilization; relapse |
| 4 | ♂ | 10 | Bilateral pyelonephritis | 88-160 | Escherichia coli | 5 grains 5 times a day* | Sterilization; relapse |
| 5 | ♀ | 4 | Bilateral pyelonephritis; cystitis | 64- 90 | Aerobacter aerogenes | 5 grains 3 times a day* | Sterilization; relapse† |

* Sodium bicarbonate given to make urine alkaline, $p_H$ 7.0+.
† Streptococcus faecalis.

TABLE 4.—*Absence of Effect on Five Strains of Streptococcus Faecalis of Urine Bactericidal for Staphylococcus and Gram-Negative Bacilli*

| Strains | Colonies in 0.5 Cc. of Urine: Before Incubation | Colonies in 0.5 Cc. of Urine: After 24 Hours' Incubation |
|---|---|---|
| 1 | 1,010 | Innumerable |
| 2 | 710 | Innumerable |
| 3 | 1,400 | Innumerable |
| 4 | 160 | Innumerable |
| 5 | 270 | Innumerable |

(table 4). Even in concentrations far above the usual bactericidal range, Streptococcus faecalis will grow.

Past experiences have shown that infections caused by Escherichia coli alone apparently cleared up under methenamine, the ketogenic diet and mandelic acid therapy, but with the disappearance of the organisms a few colonies of a streptococcus would appear on the agar plates made with 0.5 cc. of urine. In cases in which sulfanilamide was used the results have been different; in a number of instances in which Escherichia coli disappeared rapidly the urine was found to contain innumerable colonies of Streptococcus faecalis. The streptococci persisted in spite of the further use of sulfanilamide therapy but they disappeared rapidly as a result of mandelic acid therapy. Failure with sulfanilamide, as with the other urinary antiseptics, has been observed in the treatment of urinary infection associated with nephrolithiasis, postoperative wounds and indwelling catheters.

TABLE 5.—*Treatment of a Boy with Bilateral Pyelectasis, Ureterectasis and Cystitis Cystica*

| | | Dose | | | | |
|---|---|---|---|---|---|---|
| | | | Times | | | Number of |
| Days | Treatment | Grams | per Day | Pus, Grade | $p_H$ | Bacteria in 0.5 Cc. of Urine |
| | (Aerobacter Aerogenes and Escherichia Coli Infection) | | | | | |
| 1 | Ammonium mandelate.... | 1.0 | 4 | 4 | ... | Innumerable |
| 4 | Ammonium mandelate.... | 1.0 | 5 | 2 | 5.3 | Innumerable |
| 6 | Ammonium mandelate.... | 1.0 | 5 | 1 | ... | None |
| 11 | Discontinued..... | ... | .. | 1 | ... | None |
| 12 | Ammonium mandelate.... | 1.0 | 5 | 1 | ... | Innumerable |
| 17 | Ammonium mandelate.... | 1.0 | 6 | 1 | 5.2 | Innumerable |
| 19 | Ammonium mandelate.... | 1.0 | 6 | 1 | 5.5 | Innumerable |
| 22 | Ammonium mandelate.... | 1.0 | 6 | 1 | 5.0 | Innumerable |
| 25 | Ammonium mandelate and ketogenic diet..... | 1.0 | 6 | 2 | ... | Innumerable |
| 30 | Diet and ammonium mandelate discontinued.... | ... | .. | .. | ... | |
| 38 | Ammonium mandelate.... | 1.0 | 5 | 3 | ... | Innumerable |
| 42 | Discontinued..... | ... | .. | 3 | ... | Innumerable |
| | Treatment with Sulfanilamide | | | | | |
| 1 | Sulfanilamide..... | 0.33 | 4 | 3 | ... | Innumerable |
| 2 | Sulfanilamide..... | 0.33 | 4 | 1 | ... | 50 |
| 3 | Sulfanilamide..... | 0.33 | 5 | 1 | ... | 2 |
| 4 | Sulfanilamide..... | 0.33 | 5 | 1 | ... | 0 |
| 12 | Sulfanilamide..... | 0.33 | 5 | 1 | ... | 0 |
| 14 | Sulfanilamide..... | 0.16 | 5 | 0 | ... | 0 |
| 16 | Sulfanilamide..... | 0 | .. | 0 | ... | 0 |
| 19 | Sulfanilamide..... | 0 | .. | 0 | ... | 0 |
| 21 | Sulfanilamide..... | 0 | .. | 0 | ... | 0 |

Sulfanilamide is given in two-thirds the usual dosage for streptococcic infection; that is, 10 grains (0.65 Gm.) to 20 pounds (9 Kg.) of body weight is given daily. From four to six doses are given daily. Sodium bicarbonate is given in doses of from 30 grains (2 Gm.) to 60 grains (4 Gm.) a day. Water is usually given in the usual amounts, but the intake of fluids can be restricted if the concentration of sulfanilamide in the urine remains low. A concentration of 50 mg. of the drug in its free form in 100 cc. of urine is usually secured with this dosage. After the urine has become sterile it is essential to keep it so for a period of from four to six days and then discontinue medication. After an interval of four days, cultures are again taken to make sure that the urine has remained sterile. In a number of cases concentrations of half this amount have brought about sterilization of the urine. When the drug has been administered in this manner it has only exceptionally given rise to cyanosis and in my experience it never has caused agranulocytosis or anemia. It can be said definitely that, of the drugs at present available for the treatment of the types of urinary infection that have been mentioned, sulfanilamide is the most easily administered and the most useful drug except in cases in which the infection is with Streptococcus faecalis. An outline of treatment is shown in table 5.

The field of mandelic acid has been narrowed considerably by sulfanilamide, but the former drug still is very useful not only in streptococcic infections but also because of its effect on all bacteria, cocci and bacilli

TABLE 6.—*The Bactericidal Effect of Mandelic Acid on Streptococcus Faecalis at Various Concentrations and $p_H$*

| Concentration of Acid, per Cent | $p_H$ of Urine | Strains | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| 0.25 | 5.0 | — | + | + | + | + |
| 0.5 | 5.3 | S | + | + | + | + |
| 1.0 | 5.5 | + | + | + | + | + |

—, organisms not killed; +, organisms killed; S, bacteriostasis.

TABLE 7.—*Treatment of a Girl Aged 3 Years with Pyelitis of Four Weeks' Duration*

| | Ammonium Mandelate (1.5 Gm.) Four Times a Day | |
|---|---|---|
| Days | $p_H$ of Urine | Escherichia Coli |
| 1 | ... | Innumerable |
| 2 | 5.0 | 0 |
| 3 | 5.2 | 0 |
| 5 | ... | 0 |
| 6 | Medication discontinued | |
| 12 | ... | 0 |

alike; when a proper concentration of the acid in the urine and a proper $p_H$ of the urine are obtained it is a most dependable drug. As determined in vitro and therapeutically, it acts equally well in bacillary and in coccic infections. Its marked bactericidal effect on Streptococcus faecalis is shown in table 6. It is difficult to administer in the acute stage of urinary infections but its administration in enteric coated capsules and in suppositories makes it available in all cases in which acidification of the urine is possible. In Proteus ammoniae infections strongly alkaline urine and the lowered renal function render proper acidification of the urine difficult; therefore, mandelic acid is often of little use in infections of this type. In all infections in which the concentration of mandelic acid in the urine reaches from 0.5 to 1 per cent and the $p_H$ of the urine is 5.5 or less, the drug sterilizes the urine rapidly.

TABLE 8.—*Streptococcus Faecalis Infection Cured with Mandelic Acid*

| | | Dose | | | Sulfanilamide, Mg. per 100 Cc. in Urine | | Organisms in 0.5 Cc. of Urine |
|---|---|---|---|---|---|---|---|
| | | | Times | | | Conjugated | |
| Days | Treatment | Gm. | per Day | Pus, Grade | Free | | |
| 1 | Sulfanilamide..... | 0.33 | 6 | 3 | .. | .. | Innumerable |
| 2 | Sulfanilamide..... | 0.33 | 6 | 1 | .. | .. | 300 |
| 3 | Sulfanilamide..... | 0.33 | 6 | 1 | 32 | 31 | Innumerable |
| 5 | Sulfanilamide..... | 0.33 | 6 | 1 | 86 | 86 | Innumerable |
| 8 | Ammonium mandelate.. | 1.0 | 4 | 1 | .. | .. | Innumerable |
| 9 | Ammonium mandelate.. | 1.0 | 4 | 0 | .. | .. | 0 |
| 11 | Medication discontinued | ... | .. | 0 | .. | .. | 0 |
| 14 | Medication discontinued | ... | .. | 0 | .. | .. | 0 |
| 22 | Medication discontinued | ... | .. | 0 | .. | .. | 0 |

Mandelic acid is administered as the elixir of ammonium mandelate, as calcium mandelate by mouth, or as ammonium mandelate in suppositories. It is given in doses that will produce a concentration of from 0.5 to 1 per cent of the drug in the urine. At the clinic we administer 1 Gm. for each hundred cubic centimeters of urinary output in the twenty-four hours.

As most of the mandelate is excreted in the urine, a concentration of approximately 1 per cent will result. The $p_H$ of the urine can be repeatedly tested by the patient with nitrazene indicator papers. A $p_H$ of 5.5 or less is necessary for prompt action of the drug. I have repeatedly seen the urine become sterile in a period of less than twenty-four hours (table 7). It is advisable to continue the administration of the drug for five or six days after the urine has been rendered sterile, so as to kill the organisms which may be present in the various layers of the mucous membranes, and then to discontinue the medication. After an interval of four days, cultures should be taken again to make certain that the urine has remained sterile. It is well to carry out a routine such as is shown in table 8.

When the infection has been cleared up it is essential to eliminate urinary stasis if it is present. This is a matter of the utmost importance to the future health of the patient and should not be put off as it is so likely to be when the infection has been cleared up. It was possible to show with animals that so long as no stasis is present there exists an efficient barrier to the progress of an infection of the pelvis to the parenchyma of the kidney. In cases in which infection recurs periodically, it is also important to search for local foci of infection in the urethra, bladder and upper part of the urinary tract. This work should be done by a competent urologist.

SUMMARY

The diagnosis of urinary infection must include the type of infection, the state of urinary drainage and renal function, as well as the presence of foci of infection in the urinary tract. Sulfanilamide is the drug that at present meets the greatest number of conditions successfully. Mandelic acid succeeds in infections in which the necessary acidity and concentration of the drug can be obtained, including Streptococcus faecalis infection in which sulfanilamide fails. No patient should be dismissed as cured unless normal drainage is known to be present in the urinary passages.

## ABSTRACT OF DISCUSSION

Dr. William P. Herbst, Washington, D. C.: I am interested in discussing the importance of three phases of this problem of urinary infection: first, the urgent necessity for careful study of children who have had pyelonephritis; second, general resistance in infections, and, finally, the problem of myoneural dysfunctions of the bladder. Last year at Atlantic City, Wharton, Gray and Guild presented their follow-up studies on thirty young women who had had pyelonephritis in infancy or childhood and stated that six of nine who had had only one attack and eleven of twenty-one who had had multiple attacks were the victims of definite abnormalities as sequelae. These observations demand that a study be made of every child who has only a single attack of pyelitis. Abnormalities were found in 66% per cent of the children who had a single attack. During the acute attack is no time to carry out these studies. After the acute stage is over and the little patient has regained strength, the following regimen should be instituted: 1. Careful urinalysis with stain and cultural bacteriologic study. 2. Phenolsulfonphthalein excretion test following intravenous injection. 3. Check of bladder function. 4. Intravenous urography. This is not a very disturbing examination and yet it is comprehensive enough to bring to light conditions of any importance. It not infrequently happens that patients are so interesting from a diagnostic or bacteriologic standpoint that the simple problem of building up the general resistance is lost sight of. This should not be, for, after all, whether the patient survives or not depends solely on this factor. Vitamins and hematinics should be administered in generous quantities. Dr. Helmholz has pointed out the importance of obstruction, and it happens that myoneural dysfunction of the bladder is one of the most important entities in this problem. A few simple observations which any one can make quickly can demonstrate the presence of myoneural dysfunction, which should then call for a much more detailed elaborate cystometric and neurologic investigation. First, observe how the patient voids. Any abnormality of this act is very suggestive. Second, catheterize the patient with a catheter thoroughly lubricated and also small enough to minimize the resistance factor. The status of the sphincter action can be determined by the sense of resistance that is experienced. Third, determine the presence of residual urine. Lastly, observe the force of the urine as it emerges from the catheter and see at what height above the level of the bladder the flow of urine stops. Nothing could be simpler than these few homely observations and yet such an examination is adequate to recognize the presence or absence of myoneural dysfunction, which if obstructive is important in causing and continuing urinary infections.

# CHRONIC EFFECTS OF INGESTED LEAD AND ARSENIC

### A REVIEW AND CORRELATION

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The purpose of this communication is to review some of the observations presented in other papers containing the experimental details in order to correlate them with one another and with observations from the literature. Our primary interests are the comparative behavior of lead and arsenic when their salts are administered at different levels to the same species or to different species, and the correlation of physiologic and pathologic observations with results from chemical analyses.

It has been evident for some time that more extensive studies of the chronic toxicity of lead and arsenic are necessary. The growing insect infestation of fruits and vegetables has necessitated the increasing use of poisonous sprays, especially lead arsenate and calcium arsenate. The use of these has led to the serious question of whether the residues remaining on these commodities constitute a health hazard.

In formulating a law enforcement policy under the Food and Drugs Act, officials of the Department of Agriculture recognize that they were without sufficient experimental evidence to permit the establishment of wholly satisfactory tolerances for lead and arsenic. The department, therefore, in January 1927 called on a committee[1] to advise it as to just what levels of lead or arsenic content in food or drink could be considered free from hazard.

In addition to recommending temporary tolerances for lead and arsenic, this committee recommended, among other things, the study of chronic intoxication by both lead and arsenic, in particular in the form in which they are used in sprays and consumed with fruits and vegetables and other food products.

Funds for such an investigation finally became available in 1935, and a division of pharmacology was

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This is a brief summary of the work carried out in this division by a large group of investigators. The experimental procedures and results are reported separately in a series of publications in other journals.

1. This committee consisted of Drs. Reid Hunt, chairman, C. L. Alsberg, A. S. Loevenhart, Haven Emerson, Carl Voegtlin and F. B. Flinn. Dr. A. J. Carlson, although designated a member of the committee, could not attend.

established in the Food and Drug Administration. The first problem of research assigned to the division was a study of the chronic toxicity of lead and arsenic.

The Secretary of Agriculture also asked the National Academy of Sciences to appoint an advisory committee [2] on questions relating to this problem.

It was clearly recognized in the beginning that, although both forms of toxicity are caused by lead and arsenic, the question here was one of chronic and not one of acute toxicity. The real problem was to determine the minimum amounts of lead and arsenic that, when ingested periodically, would cause effects which could be attributed directly to these elements. It is clearly evident that the tolerances—that is, the amounts which may be permitted—should be below this level.

An extensive survey of the literature did not reveal the answer, although extremely valuable suggestions and helpful information were obtained. There are forty citations in the literature in which scientists have expressed themselves on the minimum amount of lead which, when ingested daily, would be dangerous.[3] Of these, eleven considered that 0.005 grain (0.325 mg.) of lead a day is dangerous, twenty-one considered 0.01 grain (0.65 mg.) dangerous, thirty-two considered 0.015 grain (0.975 mg.) dangerous, and thirty-six considered 0.02 grain (1.3 mg.) dangerous. The average American food consumption is 3 pounds (1,360 Gm.) a day. If only one third of this quantity contained the amount of lead at present permitted, it would contain, in the opinion of thirty-six of these forty authors, dangerous amounts of lead. Since the methods formerly were inadequate for quantitative determination of lead, one must consider the values mentioned by these authors in the light of present day methods and remember that there was a small amount of lead present which they did not recognize. In other words, these were the determinable values by their methods and were amounts over and above the undetermined lead. The medical and scientific literature since 1616 contains more than 10,000 references to lead and a similar number to arsenic, most of which are discussions, reports of cases and studies of acute toxicity. In no instance has it been definitely established in a single species of animal just how little arsenic or lead will cause chronic toxicity when ingested over long periods.

It will suffice at this time to cite only a few of the more important individual contributions, summaries and reviews of the literature on lead from which detailed references may be obtained. Although some experimental work was done as early as 1814, most of it has been done within the last thirty years, and excellent reviews have been published by Legge and Goadby [4] in 1912, by Oliver [5] in 1914, by Teleky, Gerbis and Schmidt [6] in 1919, by Blansdorf [7] in 1922, which alone contains about 3,000 references, and by Hamilton [8] in 1925. The contributions of Kehoe and his co-workers [9] have not been summarized. The book by Aub and his co-workers [10] contains an excellent summary and review, as well as much original work that has had an important influence on the clinical treatment of lead poisoning. The book by Nye [11] on lead and its relationship to chronic nephritis is already recognized as a classic. And, finally, there is the remarkably thorough and complete review written by Flury.[12] An excellent review of the literature on arsenic from 1846 to 1919 was published in the form of a book which consists of nineteen separate reports and contains also 106 pages of results obtained by the Swedish commission on the chronic toxicity of arsenic.[13] More recent reviews were published by Heffter and Keeser.[14]

Our problem was to determine the toxicity of lead and arsenic when used as sprays and as spray residue. Since it was essential to know the effect of lead and arsenic separately as well as in combination, we selected as salts for initial investigation lead arsenate, calcium arsenate, lead acetate and arsenic trioxide. The experimental procedures and details are published elsewhere.

## PROCEDURE AND TECHNIC

Numerous preliminary and exploratory experiments extending over a period of almost one year, not reported in this investigation but in some instances indicated, have shown that special attention must be given to methods that are sensitive for very small amounts of lead and arsenic, constituents of the diet, housing equipment and manner of feeding. We have found it impossible to select an adequate diet entirely free of lead and arsenic.

The dithizone method was extensively studied and made applicable to the determination of very small amounts of lead in biologic materials.[15]

A simple research method was developed for the determination of arsenic and applied to numerous types of food and biologic tissues.[16]

A method for the determination of the enzyme arginase was made applicable to the determination of the effects of toxic substances in general on protein metabolism.[17]

The use of a method for counting the nucleated cells of bone marrow was developed and extended.[18]

There was confirmation of the value of and extension of the use of the hydrogen sulfide technic for localization of lead, in the bones especially, as well as in

2. This committee consisted of Drs. A. J. Carlson, chairman, Torald Sollmann, Ludvig Hektoen, H. C. Sherman and Cecil K. Drinker. The committee held its first meeting in Washington, D. C., Dec. 30 and 31, 1926, and from that time on gave its services freely and ungrudgingly. Members of the committee were also available for individual consultation. Their advice and help in connection with this investigation and other problems involving the work of the division are sincerely appreciated by members of the division and by the Food and Drug Administration.

3. In this statement it is understood that the authors considering 0.005 grain of lead a day dangerous would also consider 0.01 grain dangerous and likewise those considering 0.01 grain dangerous would also consider 0.015 grain dangerous. Consequently, each succeeding number includes the immediately preceding number.

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6. Teleky, L.; Gerbis, H., and Schmidt, P.: Die Frühdiagnose der Bleivergiftung, Berlin, Julius Springer, 1919.

7. Blansdorf, E.: Biologische Schriften aus dem Gesamtgebiet der Gewerbehygiene, New Series No. 7, part 2, Berlin, Julius Springer, 1922.

8. Hamilton, Alice: Industrial Poisons in the United States, New York, Macmillan Company, 1929.

9. Kehoe, R. A., and others: Several articles published in THE JOURNAL and the Journal of Industrial Hygiene and Toxicology since 1925.

10. Aub, J. C.; Fairhall, L. T.; Minot, Anne S., and Reznikoff, Paul: Lead Poisoning, Medicine Monographs, Baltimore, Williams & Wilkins Company, 1926, vol. 7.

11. Nye, L. J. J.: Chronic Nephritis and Lead Poisoning, Sydney, Australia, Angus and Robertson, 1933.

12. Flury, Ferdinand: Lead, in Heffter, Arthur, and Heubner, Wolfgang: Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer 2:1575-1889 (pt. 2) 1934.

13. Arsenikkommissionen Betänkande, Uppsicka, Forbrygga och Motverka Faran ave Kronisk Arsenikförgiftning, Lund, 1919.

14. Heffter, Arthur, and Keeser, E.: Arsen und seine Verbindungen, Handbuch der experimentellen Pharmakologie 2:463-532 (pt. 1) 1927. Keeser, E.: Arsen und seine Verbindungen, Handbuch der experimentellen Pharmakologie 2:163-197 (suppl.) 1937.

15. Laug, E. P.: The Application of the Dithizone Method to the Determination of Lead in Biological Materials, J. A. O. A. C. 21:481-487 (Aug.) 1938.

16. Morris, H. J., and Calvery, H. O.: Quantitative Determination of Arsenic in Small Amounts in Biological Materials, Indust. & Engin. Chem. 9:447 (Sept.) 1937.

17. Lightbody, H. D.: Variations Associated with Age in the Concentration of Arginase in the Livers of White Rats, J. Biol. Chem. 124:169-178 (June) 1938.

18. Fryer, G. E., Jr.: The Concentration of Nucleated Cells in the Bone Marrow of the Albino Rat, Am. J. Physiol. 117:4 (Dec.) 1936.

other organs and tissues.[19] By this technic it can be determined whether the lead is in the nucleus of the cell or in the protoplasm surrounding the nucleus.

Glass cages, a description of which has been published,[20] were found essential for some of the phases of this investigation.

Two facts must be clearly pointed out regarding the results of these investigations: First, it must be emphasized that in all the experiments on rats, with the exception of one group, a painstaking effort was made to furnish the animals with a diet adequate in all respects, especially with regard to calcium and phosphorus. The second point which must be emphasized is that the diets fed our experimental animals were all dry diets and, especially in three of our diets, the caloric content was extremely high per gram of dry weight. This is very significant for interpretation in terms of the average human dietary, which is high in moisture. As a result of this consideration, one must keep clearly in mind that the number of grams of diet ingested by our experimental animals was relatively much less than would have been ingested had the diet had a water content comparable to that of fresh fruits and vegetables. As a result, the amounts of lead and arsenic ingested are probably from one half to one fifth as much (the lead and arsenic were expressed as milligrams per kilogram of whole diet) as would have been ingested had the animals been subsisting on diets with a water content comparable to the human dietary.

### DISTRIBUTION AND STORAGE

*Lead.*—The amount of lead stored is directly dependent on the level of intake. This was true for the range of levels studied (from 0.61 to 2,640 mg. per kilogram of diet) even at the lowest levels. For example, one group of control rats on a diet containing 0.61 mg. of lead per kilogram contained an average of 0.88 mg. of lead per kilogram of dry weight, while another group receiving a diet containing 0.73 mg. of lead per kilogram stored an average of 1.23 mg. per kilogram of dry weight. Likewise two groups of rats fed diets containing 3.53 mg. and 2,640 mg. of lead per kilogram stored respectively 1.45 and 291 mg. per kilogram of body weight.[21] Similar comparisons can be made on dogs only for individual animals. Dog 4, which was fed for 229 days the control diet containing 2 mg. of lead per kilogram, stored in the femur 77 mg. and in the kidney 7.5 mg. per kilogram of dry weight. Comparable figures for two litter mates of this dog (dogs 6 and 7) fed for 140 and 167 days a diet containing 14.8 mg. of lead per kilogram were, respectively, 469 and 506 for the femurs and 32.7 and 31.4 for the kidneys.[22]

Our investigations have shown conclusively that lead when ingested with the diet is absorbed and stored both in the skeleton and in the soft tissues, even at the lowest levels used by us in both dogs and rats. The evidence indicates that the accumulation was continuous throughout the duration of our experiments (356 days). For example, two dogs fed for 230 days on a diet containing 2 mg. of lead per kilogram stored in the femurs 68 and 77 mg. of lead per kilogram of dry weight respectively, whereas three dogs on the same diet for 350 days stored 125, 99, and 127 mg. respectively.[22] This is in agreement with the observations of Tompsett,[23] who has studied the distribution of lead in human bones. These accumulations of lead in the tissues, as demonstrated by more sensitive methods, might possibly be the cause of chronic poisoning, as well as a cumulative injury produced by small amounts of circulating lead, as postulated by Straub[24] and by Erlenmeyer.[25]

The storage of lead in the bones of young animals is much more rapid than in more mature animals. This was demonstrated very strikingly by the analyses of the femurs of a group of dogs all on the same level of lead intake (64 mg. per kilogram of diet) but placed on this diet at different ages. The average value for six young animals (from 51 to 84 days of age when placed on the diet) was 1,265 mg. per kilogram of dry weight; for two dogs about half grown (208 and 226 days of age when placed on the diet) the values were 667 and 415; for mature dogs the values were 194 and 244.[22] These differences were further emphasized by the fact that the younger dogs were on the experimental diet just half as long as were the mature dogs.

The type of diet also influences the amount of lead stored. This was clearly demonstrated in two dogs of the same litter on diets identical except for calcium content and containing 64 mg. of lead as lead arsenate per kilogram. The dog receiving 0.13 per cent calcium stored twice as much lead as the one receiving 0.28 per cent calcium. Rats placed on diets (with added lead arsenate) similar, except for calcium content,[26] showed that the animals receiving the diet low in calcium (0.13 per cent) stored in the femurs over six times as much lead as the ones on the diet high in calcium (0.53 per cent), both diets containing approximately 2 mg. of lead per kilogram. Another series of rats receiving the same respective low and high calcium diets but with 64 mg. of lead per kilogram showed that the animals fed the low calcium diet stored about five times as much lead as the others. Approximately the same ratio (about six times) held when the diet contained 512 mg. of lead per kilogram. The storage of arsenic was just the reverse of the lead but the ratios were not quite so large. Litter mate rats definitely known to be rachitic were placed at 41 days of age in pairs on the same rachitogenic diet containing three different levels of lead, namely 512, 128 and 12.8 mg. per kilogram, and were maintained on this diet for fifty days. The diet of one member of each pair was supplemented with halibut liver oil containing viosterol. The member of each pair receiving the supplement and 512, 128 or 12.8 mg. of lead per kilogram of diet stored in the femur in micrograms per gram dry weight respectively approximately 9 (1,427 and 164), 2.5 (430 and 171) and 1.6 (53 and 34) times its pair mate.[27] There was no significant difference in the amount of lead stored when the diet contained either lead arsenate or lead acetate.

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20. Lang, E. P., and Calvery, H. O.: An Improved Glass Metabolism Cage for Small Animals, J. Lab. & Clin. Med. 23:521-522 (Feb.) 1937.

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25. Erlenmeyer, Emil: Der Mechanismus der chronischen Bleivergiftung nach experimentellen Studien, Ztschr. f. exper. Path. u. Therap. 14:310-334, 1913.

26. Grant, R. L.; Calvery, H. O.; Lang, E. P., and Morris, H. J.: The Influence of Calcium and Phosphorus on the Storage and Toxicity of Lead and Arsenic, J. Pharmacol. & Exper. Therap., to be published.

27. The rachitic rats were furnished us by Dr. Rebecca Hubbell of the Connecticut Agricultural Experiment Station, New Haven. The other data are unpublished results from this laboratory.

There is storage of lead in all tissues of both species, and in some tissues the amount is enormous, especially at relatively high levels of intake. The amount stored does, however, vary, as already mentioned, with the calcium content of the diet.

*Arsenic.*—There is storage of arsenic even at the lowest level of arsenic concentration in the diet (0.07 mg. of arsenic per kilogram of diet), and a much greater storage following ingestion of diets with a higher arsenic content (215 mg. of arsenic per kilogram of diet). There was a difference in the amount of arsenic stored when different salts were fed at the same level, much more being stored when calcium arsenate was fed than when arsenic trioxide was the source of arsenic.[28] There was likewise a marked species difference, the dog storing much less than the rat, even when on the same levels of intake for longer periods of time.[22] There is a definite indication from these experiments that arsenic is not stored in anything like the amounts in which lead is stored.

The maternal transfer of both arsenic and lead as reported by other investigators [12] has been confirmed by chemical analyses of a large number of rats at birth, and of dogs. Chemical analysis has also demonstrated a higher content of lead in the milk of a dog receiving added lead in the diet than in that of a dog on a diet containing no added lead.[22] The lead content of rats at birth was the same per gram of dry weight as at 15 days of age (at this age they had not partaken of food other than the mother's milk), although their increase of weight was more than 500 per cent. This was not true for the arsenic content, which was from five to ten times greater per gram of dry weight at birth than at 15 days of age.[29]

Although in this series of investigations we have studied only the retention of lead and arsenic in two species of animals, quite extensive studies have been reported in the literature of storage in other species and in human beings. The distribution and storage of lead is fully considered by Aub and his co-workers,[10] Flury,[12] Legge and Goadby,[4] Nye,[11] Behrens and Baumann,[30] Tompsett [23] and Kehoe and his associates.[9] The last named authors have made a very significant study on man.[31] On two different occasions they studied the lead balance of an individual before lead was fed. One mg. of lead was given daily during a period of ten days, and the urine and feces were analyzed for the following sixteen days. The total lead ingested, including that in the food, was 14.2 mg. The lead retained was 4.52 mg., or 31.9 per cent of that ingested. In the second experiment, 5 mg. of lead was ingested daily for six days, a total of 30 mg. of added lead plus 2.3 mg. in the diet. The feces and urine were analyzed for thirty days before and for sixty-four days following the ingestion. The amount of lead retained was 7.62 mg., indicating quite clearly that the tissues held tenaciously to a considerable portion of the lead presented to them. This is extremely important, in view of the fact that Aub and his co-workers [10] and others [32] have shown that immobile stores of lead may be rendered mobile by alterations of the diet and by this means acute attacks of lead intoxication may be caused.

The paper of Dr. Kehoe and his co-workers,[33] which indicates that an equilibrium is established under certain conditions when the lead intake of individuals is controlled, is an excellent type of experiment. In this type of experiment, like that in which one is accurately controlling the fluid intake of individuals when one is determining water balance, it is required that extreme care be taken to measure all intake and all output. This is especially true when one is considering small differences between intake and output. The storage of lead on very low intake would be expected to be very small and, as a result, extreme care should be taken to know every source of possible intake and the amounts. In the experiment of Kehoe and his co-workers, the lead intake in the water was not mentioned, although it may have been considered with the food, and likewise the individuals were not housed during the experiment in such a way that the lead content of the inhaled air could be taken into consideration. Cursorily these sources of lead might seem of little significance, but when one is discussing equilibrium one must inevitably consider all factors. Numerous analyses of city water have shown that lead is always present. What we have analyzed averages 3 micrograms per liter, and lead from this source alone would lead to an intake of from 6 to 12 micrograms a day or probably more. Because of the lead content of the dust of the air even in air conditioned rooms, we were unable to do accurate lead balance experiments on animals when the lead intake in the food was from 0.61 to 3.53 parts per million.[21] In this connection the increasing storage of lead with age in the femur of human beings as shown by the investigations of Tompsett [23] are of particular significance, as are also the results of our investigation on animals.

## PHYSIOLOGY

*Growth.*—The effect on growth was studied only in the rats. There was no significant effect caused, we feel, by the levels of arsenic fed. In the case of lead (with adequate calcium in the diet) there was an effect on growth of the males attributable to added lead at each level. This was true at only one level for the females, in which case they were the offspring of a parent generation which had been fed a diet with the same added level of lead. With no great effects at the very high level of 2,640 mg. per kilogram of diet, it is surprising that the results are statistically very significant in the case of males fed diets containing 3.53 mg. of lead per kilogram. As would be expected, the relative amount of lead absorbed and stored by animals on the two diets was much higher for those on the 3.53 mg. level. This is in agreement with the observations of Sollmann,[34] who reported that very low levels showed, under the conditions of his experiment, greater effect on growth than somewhat higher levels. We have no explanation to offer as to why this should be the case in our series of investigations other than the fact that the lead, which was added at the lowest level,

28. Morris, H. J., and Wallace, E. W.: The Storage of Arsenic in Rats Fed a Diet Containing Calcium Arsenate and Arsenic Trioxide, J. Pharmacol. & Exper. Therap., to be published.

29. Morris, H. P.; Lane, E. P.; Morris, H. J., and Grant, R. L.: The Growth and Reproduction of Rats Fed Diets Containing Lead Acetate and Arsenic Trioxide and the Lead and Arsenic Content of Newborn and Sucking Rats, J. Pharmacol. & Exper. Therap., to be published.

30. Behrens, Behrend, and Baumann, Anny: Zur Pharmakologie des Bleis: X. Mitteilung: Die Beziehung der Bleiablagerung zum Calciumstoffwechsel, Ztschr. f. d. ges. exper. Med. 90: 251-264 (Sept.) 1933.

31. Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: On the Normal Absorption and Excretion of Lead: II. Lead Absorption and Lead Excretion in Modern American Life, J. Indust. Hyg. & Toxicol. 15: 273-288 (Sept.) 1933.

32. Gray, Irving: Recent Progress in the Treatment of Plumbism, J. A. M. A. 104: 200-205 (Jan. 19) 1935.

33. Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: Normal Absorption and Excretion of Lead: J. A. M. A. 104: 90-93 (Jan. 12) 1935.

34. Sollmann, Torald: Studies of Chronic Intoxications on Albino Rats: VI. Lead Carbonate, J. Pharmacol. & Exper. Therap. 39: 375-384 (June) 1922.

was in the form of lead arsenate, while at all other levels the added lead was in the form of lead acetate. However, our results [29] show that calcium arsenate and arsenic trioxide did not have this effect, while it was shown that lead acetate and lead arsenate were equally toxic to dogs at the levels fed.[22]

*Food Intake.*—The effect on food intake of added lead and arsenic to diets fed young rats is comparable to that found for growth. There was, in many of the experiments, a restricted food intake caused by the added lead in the diet, especially at the higher levels. This was also true for the diets containing arsenic and was especially marked at high levels. We have not enough data to determine definitely whether there was a different food intake when lead acetate was compared to lead arsenate, except at very high levels. Under those circumstances there is much greater restriction and a much greater effect when lead arsenate is present than when lead acetate is present. The effect on food intake of dogs was shown only in the case of lead. The levels of arsenic fed produced no effects. Anorexia, however, was one of the early symptoms of the effects of lead on the animal.

*Reproduction.*—Rats: Reproduction was studied most extensively in rats.[29] This was followed through four litters of the first generation and one litter of the second generation. The studies were made on equal numbers of paired litter mate experimental and control animals, and observations were made on the number of litters born, the average number of young in each litter, the survival and weight gains and the weight gains and food consumption of the dams. There was no significant difference noted in the fertility and fecundity between the experimental and the control rats. Nor was there any significant effect noted on the ability of the dams to rear their young or in the mortality up to the time of weaning at 21 days of age. The dams consumed essentially the same amount of food during the lactation period in all the groups, and their weights remained practically constant during the lactation period.

*Dogs.*—The effect on reproduction in dogs was noted only in two instances.[22] In the first instance, a mature female which had previously given birth to a litter of six pups was again bred after she had been on a diet containing added lead acetate for only one week. Even though the mother, near the end of the gestation period, showed mild symptoms of lead poisoning, six apparently normal pups were born. In the second instance a young female was bred which had, as a pup, shown severe signs of lead poisoning in the form of paralysis. She had been removed from the lead diet for an interim period of 212 days and was then returned to the lead-containing diet for approximately eighty-five days before being bred. At the end of the gestation period, when she failed to give birth to pups, she was killed, and on examination of the uterus definite evidence was found of resorbed fetuses. Although this is a single instance, it is in accord with the generally accepted view that in human beings lead shows its influence in pregnancy in a similar manner or by abortion.

## ENZYMOLOGY

In conjunction with the other studies made in this investigation, the effect of lead and arsenic on an enzyme system was included. This system was the arginase system of the rat's liver.[17] It was selected because of the generally accepted view that it is directly involved in intermediary protein metabolism, specifically in the formation of the end product, urea. By this means it was felt that if there was an effect on protein metabolism caused by the ingestion of lead and arsenic it could be indirectly measured by study of the concentrations of this enzyme, since the liver arginase concentrations following daily intraperitoneal injections of lead or arsenic were less than those of controls. Animals that had had their general metabolism interfered with by fasting showed a lower rate of protein catabolism, as measured by arginase concentration, when given lead or arsenic. Animals that had been given small quantities of lead with their food over long periods of time also showed a lower rate of protein catabolism after fasting. This was not true of animals fed foods containing arsenic. The concentrations of the enzyme in the livers of sucklings whose mothers were fed foods containing lead and arsenic were found to be significantly lower than those of controls whose mothers were fed similar foods containing no lead or arsenic.

## TOXICOLOGY

*Lead.*—The toxicology of lead has been extensively discussed by Aub and his co-workers,[10] by Flury,[12] by Nye [11] and by Legge and Goadby,[4] as well as by other investigators.[35] In our investigations, signs of lead intoxication were exhibited in both species of experimental animals but were most marked in the dogs. These animals exhibited many of the usual symptoms recognized in cases of human lead poisoning. Quite often they were restive or moody, showed loss of appetite, irritability, tremors and twitchings, paralysis from the mild to the severe forms and encephalopathy with severe convulsions. In some cases there was hematuria, and the blood changes noted were the increase of reticulocytes, stippled cells and anemia. These responses were noted both with lead acetate and with lead arsenate and at the lowest level of added lead, namely 12.8 mg. (total 14.8 mg.) per kilogram of diet, or only five times the present tolerance specified by the government, in which case the animals received only 0.33 mg. of lead per kilogram of body weight daily. As evidence of lead intoxication in the rats, very few of the usual symptoms were observed, among which were anemia, stippled cells and restricted food intake. As already mentioned, a survey of the literature revealed that thirty-six of forty investigators considered 1.3 mg. of lead per day to be dangerous for human consumption. In this connection, Sollmann [34] has made the following statement:

> These data show that daily doses of 0.01 to 0.03 mg. per kilogram are said to produce poisoning in man, but with doubtful data. Absorption of 0.1 mg. per kilogram per day from hypodermic injections does not poison cats, even in twenty-four weeks (Erlenmeyer).
>
> Daily absorption of 0.2 to 0.3 mg. per kilogram appears to be the usual dosage in human lead epidemics from leaden waterpipes, where the dosage can be rather definitely calculated from the lead content of the water (12 to 20 mg. of lead per liter; Brouardel).
>
> Daily absorption of 1 to 1.5 mg. per kilogram (from hypodermic deposits of lead carbonate, Erlenmeyer and Straub) is the smallest dosage that has been shown to produce definite symptoms in animals. The symptoms occur after a latent period of about five weeks but rapidly become severe and terminate with death; i. e., they are much more severe than the symptoms of most clinical cases.

35. Hanslik, P. J.: Health Hazards of Chemo-Enemies in Contaminated Foods, Scient. Monthly 44:435-439 (May) 1937.

Daily dosage of 12 to 30 mg. per kilogram is the smallest that has been reported as producing definite symptoms in animals, by oral administration.

In our investigations on dogs in no instance did dogs receive more than 2.56 mg. of lead per kilogram of body weight daily (and this in only one instance), following which the animal succumbed on the fifteenth day of the experiment. In view of our results, it seems that the relative toxic dose for dogs of ingested lead is approximately the same as that which had been reported for human beings who have ingested lead in their drinking water. The difference observed between the relative effects of lead on rats and dogs undoubtedly is for the great part due to the fact that the rats were on what was considered an adequate diet in all respects for growth and reproduction, whereas the dogs were on a diet considered adequate except for calcium, which was purposely made relatively low for comparison of the effects resulting when a diet was used comparable in calcium content to that of a relatively large percentage of the average human dietary. The observations of Aub and his co-workers on clinical cases, as well as in animals,[10] and our own preliminary observations had shown that there was a close relationship of the toxicology of lead to calcium metabolism. This was confirmed in experiments on both dogs and rats. From our results there is a definite indication that high levels of calcium in the diet exert some prophylactic effect with regard to lead intoxication, but it should be strongly emphasized that the hazard should be kept at a minimum and no attempt made to offset it by means of a possible prophylactic.

In many toxicologic investigations the deleterious effects of a substance are measured by its effect on growth and intake of food. Throughout this series of investigations we have been strongly impressed with the inadequacy of these criteria as measures of intoxication, since in many instances recognizable and even severe effects on the animal have been produced without noticeable alteration of these two factors. This is most marked by microscopic observation of kidneys of both rats and dogs receiving ingested lead, as well as by determination of the marked differences in weights of different organs in these animals and by chemical examination, especially of kidneys and bones. In confirmation of the attempt by Nye[11] to correlate nephritis with exposure to lead of a large proportion of the population of Australia, we have found that the organ most seriously affected by the ingestion of lead is the kidney. It should be emphasized that accurate chemical analysis of organs, tissues and body fluids is the best and probably the only adequate method at the present time of detection of exposure to lead. The development of adequate methods for determination of very small amounts of lead is probably the greatest advance that has been made in recent years for the diagnosis of lead poisoning.

*Arsenic.*—The toxicology of arsenic for both animals and human beings, and particularly the latter, is extensively discussed in practically all textbooks of pharmacology and toxicology, as well as in numerous summaries and reviews. Our investigations on arsenic have not been extensive enough to draw many definite conclusions. We have found, however, that the toxicity of arsenates, as measured by the ingestion of calcium arsenate, is greater than that of arsenites as measured by the ingestion of arsenic trioxide when consumed under the same experimental conditions and at the same level.

## PATHOLOGY

The pathologic observations on dogs and rats, so far as they have been made, are similar in many respects to those reported by other investigators as a result of the administration of these two metals both in human beings and in laboratory experimental animals. The gross pathologic changes following administration of lead included anemia, stippling of red cells, hyperplasia of the bone marrow, thickening of the bones and increased hardness and brittleness, hyperemia and edema of the brain, hypertrophy of the kidneys, due both to edema and to actual hypertrophy of the tissues as demonstrated by increased dry weight. These were associated with peripheral paralysis, severe encephalopathy, convulsions and ophthalmoplegia.[36] By special methods of treatment the deposits of lead were converted to lead sulfide, and enormous quantities were demonstrated in the bones and cartilages, and large deposits were also seen in the kidneys. These observations have been confirmed by chemical analysis. The kidneys of the rats showed marked irregularity of the tubular epithelium with hypertrophy of the nuclei of many of the tubular epithelial cells. Many of these cells contained eosinophilic inclusion bodies similar to those described by Blackman[37] in the kidneys of human subjects with lead poisoning. Special treatment of the kidneys with hydrogen sulfide revealed particles of lead sulfide in the nuclei which were similar in size and position to the eosinophilic inclusion bodies previously mentioned.

It is believed that these two types of inclusion bodies may have the same origin. Similar observations were made on the dogs, except with regard to the tubular changes. Marked tubular degeneration was found in the kidneys of all the dogs examined. The type of degeneration was different, however, from that seen in the rats. The tubular epithelial cells were irregular in size, and many contained hypertrophied nuclei. Many injured epithelial cells had sloughed into the lumen. The tubular changes noted in dogs differed from those noted in the rats and observed by Blackman in the kidneys of children who had died of lead poisoning in that no eosinophilic inclusion bodies were noted. On the other hand, the damaged nuclei were broken into many fragments which were scattered throughout the cell. Many of the tubular epithelial cells were damaged in this way, and the changes were the same in material fixed with solution of formaldehyde and with Zenker fluid. The few pathologic observations made on rats receiving arsenic revealed more or less generalized capillary dilatation in the viscera and parenchymatous degeneration of the liver. The bone marrow was slightly hyperplastic. The pathologic effects noted in the animals fed calcium arsenate were similar to those receiving arsenic trioxide, except that they were more marked and included an extensive edema. This is contrary to the usual conception that arsenic in the trivalent form is more toxic than in the pentavalent form.

## CONCLUSIONS

One of the most extensive studies made was the determination of storage and distribution of lead and arsenic in the organs and tissues of the animals when

36. Aub, Fairhall, Minot and Reznikoff,[a] Flury.[b]
37. Blackman, S. S.: Intranuclear Inclusion Bodies in the Kidney and Liver Caused by Lead Poisoning, Bull. Johns Hopkins Hosp. 58: 384-403 (June) 1936; Lesions of Lead and Encephalitis in Children, ibid. 61: 1-61 (July) 1937.

fed basic diets of known composition and the same diets to which known amounts of these elements were added. The concentrations of these in the diets ranged from a fraction of a milligram to several hundred milligrams per kilogram. There was definite storage of lead in all organs and tissues examined at all levels fed. The storage of arsenic was also shown, even at the lowest levels fed.

It was established that there are species differences in susceptibility to the toxicity of these deleterious substances.

One of the original plans of this investigation was to vary the concentration of certain essential constituents of the diet in order to determine whether such variation had an influence on the toxicity of these elements. This was considered essential because of the inconstancy of the human dietary. During the course of the study it was strikingly and conclusively demonstrated that variation of the calcium content from a low level approximating that of a large percentage of the human dietary to a higher level markedly influences the storage and toxicity of lead, and it was also demonstrated that a variation in the calcium to phosphorus ratio influenced the storage of arsenic.

At the levels fed in this investigation, calcium arsenate was more toxic and caused greater storage than did arsenic trioxide at the same level.

There was no difference observed in the toxicities of lead acetate and lead arsenate when fed at the same relatively low levels, but at high levels the lead arsenate was the more toxic.

Even at the lowest level of added lead (2.566 parts per million, total 3.53 parts per million), there was a significant effect on the growth rate of male rats and on both males and females at higher levels. In some cases there was also an influence on the intake of food.

No significant differences were noted between the control and the experimental rats in either the $P_1$ or the $F_1$ generations on the fertility and fecundity.

Our studies decisively proved, by chemical analysis of large numbers of newborn animals, that both lead and arsenic are transferred from the mother's tissues to the fetus and also that lead is transferred in the milk. Even at the lowest levels of the intake of lead (0.61 part per million) the average concentration of lead of a large number of newborn animals was the same as that of the mother's diet.

The pharmacologic and toxicologic effects of both lead and arsenic have been further demonstrated by pathologic changes, which have not only confirmed the chemical changes but been essential in the establishment of injuries when consumption of food, rate of growth and reproduction have failed to demonstrate them. The fact that criteria other than pathologic, although often the only ones used, may fail to disclose actual injury is sufficient evidence that histologic examinations must be relied on in all toxicologic studies.

In all the animals fed diets containing added lead there was a striking effect on the size of the kidney. This was most marked in those animals on the diets having the lower calcium content. In the case of dogs, the average wet weight of the experimental organs was 140 per cent and the dry weight 97 per cent greater than the weight of those of the controls. The kidney is one of the first organs, if not the first, to show signs of injury as a result of lead in the diet.

## ABSTRACT OF DISCUSSION

Dr. Floyd DeEds, San Francisco: The investigations reported by Dr. Calvery supply definite and objective experimental evidence which is confirmatory of the clinical results already known. This evidence is important and timely in view of the adverse statements made in certain nonmedical publications regarding the injustice done to farmers by the imposition of spray residue tolerance limits. Dr. Calvery has shown that storage of lead occurs in both dogs and cats even at the lowest levels of intake used. It is safe to predict that storage would have taken place with even lower levels, but longer exposure would have been required. Storage of lead is important because under altered physiologic conditions stored lead may be released, with a consequent streaming of lead through the tissues and resulting production or exacerbation of symptoms. This leads me to emphasize the importance of streaming of lead through the tissues. Aside from specific local effects in the storage depots, stored lead may be relatively harmless; it is removed from the body, in a sense. Not so the streaming lead. Chronic toxicity is associated with cumulative injury to vital tissues by chronic exposure to a stream of lead. Cumulative poisoning is frequently regarded as synonymous with storage. It is only natural that interested groups, such as producers of insecticides and farmers, should minimize and even deny the importance of, or occurrence of, lead and arsenic poisoning. It requires much more medical knowledge to appreciate the possibilities and potentialities of chronic poisoning than to appreciate acute poisoning, which is often more easily correlated with the causative factor. One may, however, be hopeful that even these groups will become cognizant of the dangers and more cooperative when the economic aspects of the problem become acute. In the state of Washington the accumulation of the spray materials of twenty years or more is making the land toxic to many kinds of plant life. The situation is sufficiently acute to cause the state college of Washington to seek an antidote for soil poisoning. Details on this subject were published in the *Washington Farmer* for April 14, 1938. The solution of the problem is not the setting of tolerance limits and the development of antidotes for soil poisoning. These are but temporary expedients to be used while new insecticides are developed, preferably organic compounds which will be nontoxic in themselves or will volatilize or decompose under weathering conditions.

Dr. Erwin E. Nelson, New Orleans: The background for the work of Dr. Calvery and his associates should be of interest in connection with the actual presentation of the experimental results. The problem was not to demonstrate the toxicity of lead or arsenic, which is generally recognized, but to demonstrate just how much lead or arsenic must be ingested to be poisonous. Under the present federal Food and Drug Act the secretary of agriculture is authorized to issue so-called tolerances for substances such as lead and arsenic. These tolerances are advisory figures for industry as to the level below which action will not be taken against foods and drugs passing in interstate commerce. The tolerances set for lead and arsenic, set after consultation with a committee of prominent scientists, have been much criticized, on the one hand, by certain persons concerned with the public health as being too liberal and, on the other hand, by producers of certain foods, particularly fruits, as being too severe. The problem set Dr. Calvery was to extend present knowledge to the place where it could be said with assurance just what tolerance is proper to protect the public health. Some recently reported work, in which rats were the experimental animals, showed that this species will tolerate relatively large amounts of lead. Opponents of the present tolerance have frequently cited this work as evidence that the tolerance is too severe. However, there are wide species differences, and such information as is available indicates that the human species is more susceptible than laboratory animals. Actually not a great deal of information exists as to human toxic or fatal doses, in a quantitative sense, except in the case of diethylene glycol, for which the information on man and laboratory animals is fairly complete. While the work of Calvery and his associates was

brought to an end before it was completed by a specific prohibition in the appropriations for the Department of Agriculture, the demonstration that dogs were seriously and even fatally poisoned by the daily ingestion of an amount of lead five times as great as that permitted under the present tolerance would make one hesitate to approve a lowering of that tolerance.

DR. P. J. HANZLIK, San Francisco: Dr. Calvery has essentially confirmed the results of others with lead and arsenic compounds. Residents on the Pacific slope know that 60 or 70 per cent of the insecticides used in this country are sprayed on the valleys and mountain sides and on all kinds of food products there, and they have opportunities to observe interesting aspects of the health hazard problem. When one considers these features, together with experimental results, there is not much doubt that there are health hazards in spray residues. A rancher testified that he lost 5,000 turkeys by driving them through an orchard; another rancher drove his team of horses through an orchard, where they nibbled alfalfa, and later the horses died. A pest control operator said to me "What can I use in the place of lead arsenate? I am practically broke from spraying with airplanes and having some of the spray drift to adjoining ranches and having to pay indemnities for losses of cattle." Dr. Calvery has added new evidence. He has taken great pains in examining the blood and tissues. He makes a point of the increase in size of the kidney, which agrees with the results obtained with other heavy metals and is apparently a form of nephrosis. These effects seem to occur before other general physiologic reactions. He has made experiments with lead arsenate itself and confirmed known experimental and clinical effects of lead and arsenic, as well as opinions of qualified experts given in court concerning the health hazards of spray residues. He makes the point that lead is more important than arsenic in this connection, which is correct. His positive results dispose of the uncritical results of Tayloe and Talbert of the University of Missouri Agricultural Experiment Station, who claimed that lead arsenate fed to rats was not injurious and, in fact, seemed innocuous, if not beneficial. The fact is that the quantity, or dose, or the tissue concentration and the time element are in inverse relationship: the lower the dose, or the lower the tissue concentration, the longer it takes for the development of manifestations of chronic intoxication, and the greater the dose, or the higher the tissue concentration, the shorter the time for development of functional injuries. As far as tolerance limits are concerned, any one who knows the history of this problem knows that they are purely arbitrary. Dr. Calvery has shown that five times the tolerance limit for lead, which is a very low concentration in the diet, causes definite injurious effects, and he has reason to believe that the tolerance limit itself would produce effects if the poison was given long enough, and I agree with that.

**Mauriceau's Book Used 150 Years.**—Since obstetrics was the one specialty left open to medical women in the seventeenth century, it was not unnatural that Ambroise Paré should in 1573 write a book for French midwives and open his own house as a school for their education. But his book incurred the wrath of the surgeons of Paris because, being written in French, it gave promise of being popular. They immediately jumped to the obvious conclusion that, if midwives were well educated, they could and would undertake all sorts of surgical operations which hitherto men alone had performed. As a fact, since the beginning of the century men were being frequently called by midwives to help in a difficult or operative labor case. Mauriceau (1637-1709), for instance, went not only to the Hotel Dieu to assist the midwives there with their charity patients but also to the bedside of noble ladies during their confinements. His book on the diseases of pregnancy and the puerperium, published in 1668 and illustrated with fine copper plates, was used for a hundred and fifty years until corrected and superseded by Madame Boivin's book in the early nineteenth century.—Hurd-Mead, Kate Campbell: A History of Women in Medicine, Haddam, Conn., the Haddam Press, 1938.

# NUTRITIONAL DEFICIENCY AND THE NERVOUS SYSTEM

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The phenomenal advances of recent years in the field of nutritional diseases have brought about a reorientation of thought and have made it evident that the older clinical classifications and nomenclature are sometimes misleading. For example, the term "pseudopellagra," which was based on an etiologic misconception, has been dropped by common consent, and that of "alcoholic" polyneuritis has been proved to be a misnomer.[1] Moreover, various other neuritides that were formerly attributed to some hypothetic toxin, and even certain cases of "infectious" polyneuritis, are now being attributed to deficient ingestion or utilization of the vitamin B complex.

## RECENT OPINION

In a recent paper by Cobb and Coggeshall[2] the principal causes of polyneuritis were classified as in the accompanying table.

*Generalized Polyneuritis*

| Virus | Bacteriotoxic | Deficiency or Metabolism |
|---|---|---|
| Measles | Focal infections | Pellagra |
| Smallpox | "Rheumatism" | Pernicious anemia |
| Chickenpox | Erysipelas | Sprue |
| Parotitis | Scarlet fever | Beriberi |
| Herpes | Rheumatic fever | "Alcoholic neuritis" |
| "Acute febrile" | Chorea | "Korsakoff's psychosis" |
| "Acute infective" | Septicemia | Pernicious vomiting |
| "Landry's" | Puerperal fever | Hunger edema |
| Poliomyelitis | Gonorrhea | Pregnancy |
| Encephalomyelitis | Meningitis | Chronic colitis |
| Epidemic (lethargic) encephalitis | Diphtheria | Cancer with cachexia |
| | Typhoid | Tuberculosis with cachexia |
| Erythro-edema | Paratyphoid fever | Senility with cachexia |
| Acute rabic myelitis | Typhus fever | Diabetes |
| | Influenza | Myxedema |
| | Pneumonia | Hemoglobinuria |
| | Malaria | "Recurrent polyneuritis" |
| | Relapsing fever | "Chronic progressive polyneuritis" |
| | Serum sickness | |
| | Acute enteric fever | Chronic bacillary dysentery |

This classification of Cobb and Coggeshall includes under the heading of "deficiency or metabolism" a large series of neuritides which would not have been so classified a few years ago. Therefore is it not reasonable to suppose that increasing knowledge may lead considerably further in the same direction? For example, why did not Cobb and Coggeshall include in the column of neuritides attributable to "deficiency or metabolism" cases developing in relation to malaria, the enteric fevers, typhus fever and, perhaps, still others which they classified as "bacteriotoxic?" The views recently expressed by several other authors are illuminating in this connection:

Wechsler[3] said (p. 825):

> Many cases of polyneuritis of obscure origin are probably neither toxic nor infectious in nature, at least not in the sense in which those two words are generally used, but more likely are deficiency syndromes. Even if, from their clinical appearances they cannot be regarded as cases of beriberi or pellagra,

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1. Minot, G. R.; Strauss, M. B., and Cobb, Stanley: "Alcoholic" Polyneuritis; Dietary Deficiency as a Factor in Its Production, New England J. Med. 208:1244 (June 15) 1933. Strauss, M. B.: The Etiology of "Alcoholic" Polyneuritis, Am. J. M. Sc. 189:378 (March) 1935.

2. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, J. A. M. A. 103:1608 (Nov. 24) 1934.

3. Wechsler, I. S.: Etiology of Polyneuritis, Arch. Neurol. & Psychiat. 29:813 (April) 1933.

they might still be grouped with the avitaminoses. . . . In many cases of polyneuritis which have hitherto been regarded as due solely to a specific cause, such as alcohol, lead, arsenic or phosphorus, one finds an additional, possibly determining, factor in avitaminosis. This may be due to involvement of the gastrointestinal tract or the liver, of which there is not infrequently clinical evidence. Such a view may serve to explain why polyneuritis develops in only certain patients, although all are exposed to the same poison. . . . The fact that the general pathologic changes are degenerative rather than inflammatory and are similar to the degenerative changes seen in avitaminoses furnishes pathologic evidence of some value. . . . While in beriberi and pellagra the antineuritic vitamins $B_1$ and $B_2$, or G, are involved, in some obscure cases and in some others in which the avitaminosis seems to play the decisive role it may be that other or additional vitamins are concerned. . . . It is possible . . . that in every case in which there is a deficiency of antineuritic vitamins there must be an additional toxin or poison to bring about degenerative changes.

The growing tendency to group together neuritides that have been described as separate types is also illustrated in a paper by Harris.[4] He suggested that various forms of recurrent or progressive polyneuritis, excepting Dejerine's familial type, should be regarded as variations and should be brought together under the descriptive term of "chronic progressive (endotoxic) polyneuritis."

Lewy[5] writes as follows:

This presentation, which is based on clinical observations and neurologic and chemical examinations, started with the observation that, despite the clinical variety of peripheral nerve diseases, their histopathologic features are uniform. Primary inflammatory processes of the peripheral nerves are unknown. Therefore the term neuritis is erroneous and should be replaced by neuropathy. . . . The pathogenic mechanism of the neuropathy, therefore, seems to be as follows: First, various primary etiologic agents—infectious, toxic and metabolic—act on the liver. The liver cell becomes depleted of its glycogen and, simultaneously, of its vitamin B content. Then the stage is set for a neuropathy. Second, avitaminosis B appears as the only form of neuropathy. However, the neuropathy is not the only sign of avitaminosis B. In addition, there are (1) the so-called general symptoms, (2) physical signs and (3) evidence of systematic degeneration in the spinal cord and basal ganglia. The same phenomena have been found and discussed in connection with the following groups of diseases: (1) disturbances of metabolism, e. g. in diabetes, alcoholism, pregnancy, cachexia and hunger; (2) pernicious anemia; (3) poisoning with heavy metals, such as lead, manganese, arsenic and mercury; (4) infectious diseases, e. g. yellow fever, typhus, typhoid and paratyphoid, streptomycosis and diphtheria, and (5) some constitutional hereditary forms of neuropathy.

A number of interesting points were raised in the discussion of a subsequent paper by Lewy.[6] Zimmerman[7] said at that time:

Which chronic alcoholic patient will present clinical manifestations of pellagra and which the polyneuritis of beriberi cannot be predicted. Nor can one predict the type of anatomic changes in the nervous system. I have seen several such patients, each of whom had "axonal" changes in the ganglion cells like those associated with pellagra, pseudo-encephalitic lesions of Wernicke, degeneration of the posterior columns of the cord and demyelination of peripheral nerves.

The views and postulates of Cobb and Coggeshall, Wechsler, Lewy and Zimmerman as here epitomized show that vitamin deficiency should now be seriously considered as a factor of possible importance in the mechanism of production of a great many cases of degeneration of the peripheral nerves, with or without evidence of cord lesions, which would have been attributed in former years to various other causes.

In this connection, I believe that to Cobb and Coggeshall's list of neuritides attributable to "deficiency or metabolism" might properly have been added some of the neuritides listed by them as "bacteriotoxic." I refer especially to neuritides occurring in typhus fever, malaria, relapsing fever and the enteric fevers. The well known increased need for vitamins that occurs in the presence of infections is a point in favor of this view. In a paper published ten years ago I[8] showed a close analogy between the polyneuritis of beriberi and that occurring in alcoholism and in debilitating diseases of many kinds. It was said then that "some of the cases of polyneuritis developing with the above-mentioned conditions might, perhaps, be properly regarded as true beriberi and not merely as complications or sequelae of the other diseases."

In 1936 Vedder[9] (p. 292) made the following significant statement:

Beriberi may be associated with other diseases, such as malaria and the various intestinal and pulmonary infections. Bronchopneumonia frequently is found at necropsy. It is an interesting speculation if the neuritis attributed to malaria, dysentery and other infections may not in many instances be caused by mild symptoms of beriberi. Certainly, neuritis complicating the various infections is seen more commonly in Oriental races than among Europeans. Many of these infections also are chronic and are treated with one-sided or liquid diets.

Substances contained in the vitamin B complex are known now to be of essential importance for the protection of the nervous system. It is generally recognized, too, that failure to assimilate and to utilize these substances may be as potent a cause of neurologic pathologic changes as is failure to ingest the vitamins in adequate quantity.

This concept permits the classification, as syndromes of deficiency of vitamin B, the neuritides occurring in connection with a great variety of morbid conditions.

## PATHOLOGIC CHANGES OF THE NERVOUS SYSTEM IN DEFICIENCY DISEASES

The point should be emphasized here that lesions may be found in the nervous system showing cellular infiltration about the blood vessels or other phenomena which are commonly associated with, and attributable to, inflammation caused by infectious processes. There are also degenerative lesions traceable to arteriosclerosis. The frequent finding of arteriosclerotic changes in the brains of elderly pellagrins, however, does not invalidate the fact that degenerative changes have been frequently described as occurring in the brain in cases of pellagra in which there was no associated arteriosclerosis. I shall discuss only lesions of a degenerative or "neurotoxic" character which are not complicated by evidences of inflammation or arteriosclerosis.

*Beriberi.*—According to Vedder,[9] the degenerative changes in the peripheral nerves may be slight or pronounced, but all peripheral nerves commonly show some

4. Harris, Wilfred: Chronic Progressive (Endotoxic) Polyneuritis, Brain **58**:348 (Sept.) 1935.
5. Lewy, F. H.: The Problem of Neuritis, Arch. Neurol. & Psychiat. **39**:222 (July) 1937.
6. Lewy, F. H.: Neurologic Aspects of B Avitaminosis, Arch. Neurol. & Psychiat. **39**:650 (March) 1938.
7. Zimmerman, H. M., in discussion on Lewy,[6] p. 653.
8. Shattuck, G. C.: The Relation of Beriberi to Polyneuritis from Other Causes, Am. J. Trop. Med. **8**:539 (Nov.) 1928.
9. Vedder, E. B.: Beriberi and Epidemic Dropsy, Oxford Loose-Leaf Medicine **4**:273 (pt. 2) 1936.

signs of degeneration. The membranes of the cord are often congested and edematous, and the cord may appear to be abnormally soft. Scattered fibers in all tracts show the same sort of changes as are found in the peripheral nerves. Degenerative changes are found also in the cells of the anterior and of the posterior horns, and in the sympathetic ganglions as well. Marked lesions in the brain have been found also by L'Hermitte (cited by Vedder). These facts have led Vedder to state that "although the symptoms of beriberi have been attributed in the past chiefly to peripheral neuritis, the condition is not a simple polyneuritis but is a degeneration of the entire nervous system as well as of other organs."

Very recently, Vedder [10] has said that degenerative changes in the cord are seen particularly in the posterior columns as well as in the anterior and posterior nerve roots and that similar changes have been found in the ganglion cells of the medulla and pons as well as in the cranial nerves, particularly the phrenic and the vagus.

Of infantile beriberi, Vedder said that the degenerative changes in the nerves are usually less marked than in adult cases and that this may be because the disease is apt to be of shorter duration in infants.

According to Manson-Bahr [11] (p. 406) the cranial nerves above the seventh are rarely involved in beriberi but, in some cases, the laryngeal muscles are paralyzed. Laryngeal paralysis is believed to be relatively common in the infantile form of beriberi, but this symptom has been attributed by some persons to an effect of pressure on the left laryngeal nerve exerted by a dilated right auricle.[11a]

It is interesting to note here that Brown [12] believes that in the case described by Landry,[13] from which were derived the terms "Landry's paralysis" and "Landry's syndrome," death was due to beriberi. I agree with this view and, further, that an important group of cases which can properly be designated as Landry's paralysis or Landry's syndrome are due essentially to deficient ingestion or utilization of components of vitamin B.[14]

Moreover, a close relationship between Korsakoff's syndrome and beriberi seems now to have been established. At any rate, it seems to have been proved that widespread degenerative lesions of the nervous system occur in typical cases of beriberi and that such lesions have been found in nearly all parts of the nervous system, including the brain.

*Korsakoff's Syndrome.*—In 1890 Korsakoff [15] reported six cases of psychosis that were associated with polyneuritis. In four of these cases there was no evidence of alcoholism and, in the other two cases, it was not clear that alcoholic beverages had been taken to excess. Korakoff's syndrome, therefore, is not dependent on a background of alcoholism. No autopsy reports were included in the paper of 1890, but Korsakoff referred to two other papers published by him in Russian in 1887, which dealt respectively with "atrophic spinal paralysis and multiple neuritis" and with "alcohol paralysis." [16] He was impressed with the similarity between the conditions seen in alcoholic addicts and those not addicted to alcohol, and he expressed the view that alcohol merely facilitated the action of some other toxic substance.

Korsakoff [15] (p. 693) said also in 1887 that the peripheral nerves are by far the most frequently damaged but that the spinal cord and brain frequently suffer also. It was not clear to him why such differences should occur, but he pointed out that, in alcoholic cases, cerebral pathologic changes were almost always associated with polyneuritis.

Korsakoff and Serbski [17] published a detailed account of a case of polyneuritic psychosis with autopsy. They believed that alcohol played no part whatever in this case. Lesions were found in the peripheral nerves, and there was an increase of neuroglia in the columns of Goll as well as in the lateral columns in the cervical region. No lesions were found in the brain. Nevertheless, the authors believed that the symptoms in this case indicated an effect on the brain, and they said that, as in many other cases of multiple neuritis, there is reason to believe that the cause of the disorder operates on the spinal cord as well as on the brain.

Thus in Korsakoff's syndrome the lesions of the peripheral nerves, of the cord and of the brain seem to be indistinguishable from those which may be found in beriberi. I have seen a few cases of Korsakoff's syndrome in which there were cutaneous lesions suggestive of pellagra and it is well known that symptoms of polyneuritis may be associated with pellagra.

Moreover, Carmichael and Stern [18] suggested tentatively that "a common factor may operate in Korsakoff's syndrome and in pellagra, or that in these conditions there may be a deficiency in an essential factor, lack of which permits toxins to attack and damage the highly specialized nerve cells of the cerebral cortex."

A close relationship between beriberi, "alcoholic polyneuritis," Korsakoff's syndrome and pellagra, with or without alcoholism, is apparent from the clinical standpoint. What, then, are the lesions found in the nervous system in pellagra?

*Pellagra.*—Many years ago Mott [19] described widespread lesions of the nervous system in cases of pellagra. In none of his cases was there any evidence of the meningeal or perivascular cellular infiltration that is usually associated with lesions of the nervous system caused by an infecting organism. On the other hand, all the changes found were like those produced by a chronic toxemia and it was pointed out that the "combined sclerosis" of pellagra is "not unlike" that found in pernicious anemia. The pathologic changes reported by Mott were seen in all the posterior spinal ganglion cells, in all the cells of the anterior horn in varying degrees and in their homologues in the medulla and pons as well. Similar changes were observed in the Betz cells of the cortex and in the cells of Purkinje, and there was marked chromatolysis in the cells of Clarke's column. Mott characterized the lesions found as "combined sclerosis of the cord."

10. Vedder, E. B.: The Pathology of Beriberi, J. A. M. A. 110: 893 (March 19) 1938.
11. Manson-Bahr, P. H.: Manson's Tropical Diseases, ed. 10 (revised). Baltimore, William Wood & Company, 1936.
11a. Stitt, E. R.: The Diagnostics and Treatment of Tropical Diseases, ed. 5 (revised), Philadelphia, P. Blakiston's Son & Co., 1929, p. 428.
12. Brown, Madelaine R.: A Note on the Etiology of Landry's Acute Ascending Paralysis, Arch. Neurol. & Psychiat. 40: 800 (Oct.) 1938.
13. Landry, J. B. O.: Note sur la paralysie ascendante aigue, Gaz. hebd. de méd. 6: 472, 1859.
14. Shattuck, G. C.: "Landry's Paralysis" in Relation to Vitamin B Deficiency, Internat. Clin. 3: 24 (Sept.) 1938.
15. Korsakoff, S. S.: Ueber eine besondere Form psychischer Störung, combinirt mit multipler Neuritis, Archiv. f. Psychiat. 21: 669, 1890.
16. The references which he gives (pp. 691 and 693) are as follows: 1. A monograph entitled "Ueber die Alkohollähmung" (Russian), Moscow, 1887, p. 262. 2. "Zur Lehre von der Pathogenese der atrophischen Spinalparalyse und der multiplen Neuritis," Arch. Psychiat., etc., Charcot 2: 16, 1887.
17. Korsakoff, S. S., and Serbski, W.: Ein Fall von Polyneuritischer Psychose mit Autopsie, Arch. f. Psychiat. 23: 112, 1892.
18. Carmichael, E. A., and Stern, R. O.: Korsakoff's Syndrome: Its Histopathology, Brain 54: 189 (June) 1931.
19. Mott, F. W.: The Histological Changes in the Nervous System of Dr. Box's Case of Pellagra, Brit. M. J. 2: 4, 1913.

Manson-Bahr [21] said (p. 427) that, in the cord, the middle and lower thirds of the lateral columns and the crossed pyramidal tracts are especially implicated, that the direct cerebellar tracts usually escape and that there may be wasting of the brain.

A more detailed account of the pathologic changes of the nervous system in pellagra and a review of the literature can be found in an article,[20] originally written by Edward Jenner Wood (date not indicated), since revised by F. R. Taylor. The following interesting points were brought out:

1. Spiller and Anderson [21] believed that pellagra does not produce a true systemic disease of the nervous system and that degeneration is caused by some toxin that affects all parts of the cerebrospinal system.

2. Having studied thirteen cases, Wilson [22] found degeneration of the posterior tracts to be more frequent than that of the lateral tracts, but the process was never confined to any system. A marked resemblance to subacute combined degeneration was noted.

3. Cotton studied a single case of Wood's which tended to confirm his belief that the lesions of pellagra are markedly similar to those found in the central neuritis of Adolf Meyer and that there is also a resemblance between them and the chromatolysis described by Marinesco.

4. A change in the ganglion cells of the sympathetic system was observed by Roaf (Report of the Egyptian Commission).

Langworthy [23] described in detail the neurologic lesions found in a woman aged 22 who died of pellagra. He said:

> Accumulations of pigment were found in cells of the sensory and autonomic ganglia and in those in the spinal cord and brain-stem. The anterolateral columns of the cord were most severely involved; there was no abnormality in the posterior columns. The lesions involved particularly the spinocerebellar and corticospinal tracts. It is probable that the neurological abnormalities were of only short duration; considerable fat could be demonstrated in the lateral columns of the cord.

Similar studies by Susman [24] revealed complete unilateral degeneration of the dorsospinocerebellar tract in the upper thoracic region in one case, and in another case posterolateral degeneration chiefly, and slight degeneration of the direct pyramidal tracts. In one case he found perivascular pigment in the cerebrum, cerebellum and midbrain. These lesions were associated with varying degrees of degeneration of the pyramidal cells of the cortex, the Purkinje cells of the cerebellum and the ganglion cells of the midbrain.

Briefly stated, the distribution of lesions of the nervous system in pellagra is by no means uniform. Lesions of degenerative type are apt to be widespread, however, and they may be found in the peripheral nerves, the spinal cord, the medulla, the pons, the cerebellum or the cerebrum.

Although the usual distribution of the lesions in pellagra differs from that commonly seen in beriberi, the changes appear to be similar in kind. Both clinical and pathologic evidence points to a close etiologic relationship between beriberi, Korsakoff's syndrome and pellagra. Moreover, the "central neuritis" of Adolf Meyer and "subacute combined degeneration of the cord" appear to be closely linked to pellagra.

*Pernicious Anemia.*—According to Minot [25] (p. 999) the characteristic lesion in the spinal cord in pernicious anemia is diffuse subacute combined degeneration of marginal distribution. It is usually symmetric and generally it appears first in the upper thoracic and cervical portions of the cord and in the posterior columns. The dorsal roots may be attacked early and the ventral roots later. Lesions of the peripheral nerves are found also, and the brain may show degenerative changes as well.

Woltman and Heck [26] listed and discussed a great variety of morbid conditions in which this syndrome had been observed. They showed the difficulty of classifying such cases until the essential etiology has been determined. In their summary they said (p. 299):

> On the basis of a survey of the important available literature, it appears that this familiar and challenging picture may be brought about by chronic alcoholism, gastric carcinoma, obstruction and fistulas of the intestinal tract, pernicious anemia, so-called prepernicious anemia and scurvy. It possibly may be similarly related to pancreatitis, pellagra and hemolytic icterus, and it has been in some manner associated with amyotrophic lateral sclerosis and a number of unclassified diseases.
>
> An important physiologic principle appears to be involved. Careful hematologic studies, gastric analysis and an investigation of the presence of Castle's intrinsic factor, if facilities are available, possibly would lead to the disclosure of some one underlying cause, probably nutritional and in the nature of a deficiency.

Pernicious anemia is listed now among the deficiency diseases. There are striking analogies between the degenerative lesions found in the nervous system in pernicious anemia, pellagra and beriberi. Subacute combined degeneration of the cord has been found in the absence of pernicious anemia, but it has also been observed in association with many disorders in which nutrition is seriously affected, such as malaria, typhoid, typhus fever, tuberculosis, alcoholism, dysentery, gastroenteric disorders, beriberi, pellagra, pernicious anemia, scurvy and sprue.

Twelve years ago, Reed and Wyckoff [27] pointed out a close relationship between sprue, pernicious anemia and subacute combined degeneration of the cord and reported cases to support their belief. Such a relationship has since received general acceptance.

Therefore it seems highly probable that disorders of nutrition involving deficiency of vitamins of the B complex or of unknown substances contained in liver are responsible for most of the cases of subacute combined degeneration of the cord, whether or not associated with pernicious anemia.

### LESIONS OF THE CRANIAL NERVES TRACEABLE TO VITAMIN DEFICIENCY

I noted earlier that lesions of the medulla, of the vagus, of the phrenic and of other cranial nerves may occur in beriberi and that lesions of the medulla may also be found in pellagra. Many years ago, Darling [28]

20. Wood, E. J.: Pellagra, Oxford Loose-Leaf Medicine 4: 307 (pt. 2, chap. 13) 1929; revised by F. R. Taylor.
21. Spiller, W. G., and Anderson, F. V.: Pellagra with a Report of Two Cases with Necropsy, Am. J. M. Sc. 148: 94, 1914.
22. Wilson, S. A.: The Pathology of Pellagra, Proc. Roy. Soc. Med., Lond., Neurol. Sec. 7: 31 (No. 4) 1914.
23. Langworthy, O. R.: Lesions of the Central Nervous System Characteristic of Pellagra, Brain 54: 291 (Sept.) 1931.
24. Susman, William: Morbid Anatomy and Histology of Pellagra, Tr. Roy. Soc. Trop. Med. & Hyg. 24: 23 (June) 1930.
25. Minot, G. R.: Pernicious Anemia, in Cecil, R. L.: Textbook of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1937.
26. Woltman, H. W., and Heck, F. J.: Funicular Degeneration of the Spinal Cord Without Pernicious Anemia, Arch. Int. Med. 60: 272 (Aug.) 1937.
27. Reed, A. C., and Wyckoff, H. A.: The Common Picture of Sprue, Pernicious Anemia, and Combined Degeneration, Am. J. Trop. Med. 6: 221 (May) 1926.
28. Darling, S. T.: The Pathologic Affinities of Beriberi and Scurvy, J. A. M. A. 63: 1290 (Oct. 10) 1914.

reported finding degenerative changes in the vagus nerve in certain cases of scurvy. Moreover, he stated that the lesions of the cardiac muscle which he found in scurvy were of the "same type" as those seen in beriberi. Now that combined deficiencies are known to be common, Darling's cases might be interpreted as instances of deficiency of vitamin C combined with that of vitamin $B_1$.

Taylor and McDonald [29] suggest that the facial nerve may also become involved in severe cases of beriberi. These authors say in their conclusion (p. 243):

> The etiology [of the syndrome] has not been definitely determined. The signs of infection are slight and often entirely absent. A febrile onset is inconstant. . . . The symptomatology, apart from the somewhat arbitrary coincidences of facial diplegia and general peripheral neuritis or neuronitis, is varied. No constant relationship exists between the appearance of the facial paresis and the more general signs of neuritis. . . . Pathologic changes are of the nature of a diffuse inflammation involving especially peripheral neurons, the cord and brain stem to a lesser extent and the cortex slightly if at all. The cerebrospinal fluid varies from normal to a condition characterized by a pronounced increase in total protein with slight or often no increase in the number of cells.

It appears from the foregoing that changes indicating the presence of an infectious process were present in some of the cases discussed by Taylor and McDonald but were entirely absent in others. The propriety of characterizing the changes observed in the peripheral nerves as being in the "nature of a diffuse inflammation" is open to question. With regard to this matter, Lewy [5] (p. 222) said: "Primary inflammatory processes of the peripheral nerves are unknown. Therefore the term neuritis is erroneous and should be replaced by neuropathy." Probably, Taylor and McDonald's paper deals with cases belonging to two entirely different categories, namely (*a*) infectious diseases involving the central nervous system and (*b*) degenerative processes attributable to deficiency of vitamin $B_1$.

In 1931 Keefer [30] listed among the clinical features of vitamin B deficiency aducens palsy, facial palsy and retrobulbar neuritis.

Reviewing the subject of nutritional diseases of the eye, Benedict and Wagener [31] listed among them retrobulbar neuritis, optic neuritis and paralysis of the ocular muscles. The same subject was discussed by Fine and Lachman,[32] and Moore [33] pointed out that retrobulbar neuritis followed by more or less optic atrophy is common in pellagra and that this fact has not been fully appreciated. Cohen [34] has called attention to the fact that visual disturbances and optic atrophy may precede other neurologic and blood changes in pernicious anemia and that the lesions yield to liver extract when treated early.

Carroll [35] reported ten cases of "alcohol" amblyopia which occurred in patients who had pellagra or polyneuritis or both. All were heavy drinkers. In every case, he said, the diet had been inadequate. In the following year Carroll [36] stated that nutrition apparently plays an important role in tobacco-alcohol amblyopia and reported on a small series of cases in which satisfactory improvement occurred on an adequate diet high in vitamin B without diminishing the amount of alcohol previously taken or the tobacco used.

Laryngeal paralysis has already been mentioned as occurring occasionally in beriberi, but the significance of this symptom is uncertain.[11a]

A possible relationship between "chronic progressive deafness" and deficiency of vitamin $B_1$ has been suggested by Selfridge.[37]

The contributions of the authors quoted serve to emphasize the fact that lesions of various cranial nerves may be associated with a number of different deficiency syndromes.

## LESIONS OF THE BRAIN

Without undertaking a discussion in detail of the lesions of the cerebrum which accompany known deficiency syndromes, it may nevertheless be worth while to point out that cerebral lesions of the "degenerative type" have been described for beriberi, pellagra, Korsakoff's syndrome and pernicious anemia. Moreover, cerebral symptoms and psychic disorders may be associated with any of these diseases.

Various types of changes in the brain in cases of cachexia associated with gastrointestinal infection have been described by Alexander and Wu.[38]

It is well known that the type of psychic disorder which commonly appears in the later stages of pellagra is, in some cases, the presenting symptom. Because this type of mental disorder is not very clearly definable, the true nature of such cases may be obscure until other more characteristic lesions appear. Therefore, is it not reasonable to infer that there are cases in which the characteristic lesions of pellagra or of some other deficiency syndrome do not develop and which, nevertheless, are caused essentially by some disorder of nutrition? If this inference is correct, the psychiatrist may ultimately come to believe that inadequate nutrition plays a far more important role in his field than has yet been assigned to it. At this point the fact requires emphasis that deficiency syndromes are not necessarily accompanied by emaciation. Certain acute cases of beriberi and of pellagra bear witness to this truth.

## SUMMARY

There seems to be adequate ground for the following inferences:

1. The lesions of the nervous system which are common in beriberi, pellagra, Korsakoff's syndrome and pernicious anemia, as well as those found in many cases of combined degeneration of the cord, in Landry's paralysis and in polyneuritis associated with a great variety of morbid conditions, are traceable to deficiency of diet or to conditions that interfere with utilization of factors contained in food which has been ingested.

2. The morbid processes so produced in the nervous system are similar in character and are often widespread.

29. Taylor, E. W., and McDonald, C. A.: The Syndrome of Polyneuritis with Facial Diplegia, Tr. Am. Neurol. A., 1931, p. 210; Arch. Neurol. & Psychiat. 27:79 (Jan.) 1932.
30. Keefer, C. S.: Some Clinical Aspects of Deficiency Diseases, New England J. Med. 205:1086 (Dec. 3) 1931.
31. Benedict, W. L., and Wagener, H. P.: Nutritional Diseases and the Eye: The Role of Vitamin B, Am. J. M. Sc. 188:296 (Aug.) 1934.
32. Fine, Max, and Lachman, G. S.: Retrobulbar Neuritis in Pellagra, Am. J. Ophth. 20:708 (July) 1937.
33. Moore, D. G. F.: Retrobulbar Neuritis cum Avitaminosis, etc., West African M. J. 9:35 (June) 1937; abstr. Trop. Dis. Bull. 35:72, 1937.
34. Cohen, Henry: Optic Atrophy as Presenting Sign in Pernicious Anemia, Lancet 2:1202 (Nov. 21) 1936.
35. Carroll, F. D.: "Alcohol" Amblyopia, Pellagra, Polyneuritis: Report of Ten Cases, Arch. Ophth. 16:919 (Dec.) 1936.
36. Carroll, F. D.: Recovery from Tobacco-Alcohol Amblyopia with Continuance of Tobacco and Alcohol, Arch. Ophth. 18:176 (July) 1937; Importance of Diet in the Etiology and Treatment of Tobacco-Alcohol Amblyopia, ibid. 18:948 (Dec.) 1937.
37. Selfridge, G. L.: Chronic Progressive Deafness from Nutritional Standpoint; Preliminary Report, Ann. Otol., Rhin. & Laryng. 46:875 (Dec.) 1937.
38. Alexander, Leo, and Wu, T. T.: Symptomatic Involvement of the Nervous System in Different Forms of Dysentery, Chinese M. J. 48:1 (Jan.) 1934; Cerebral Changes in Gastrointestinal Infections with Terminal Cachexia, Arch. Neurol. & Psychiat. 33:73 (Jan.) 1935.

3. The presenting symptoms may be traceable to almost any part of the nervous system. Therefore a great variety of clinical syndromes may result from deficiency states.

4. Neurologic lesions caused essentially by deficiency are usually traceable to lack of a part or parts of the vitamin B complex or of something contained in liver.

5. Many neurologic syndromes which have not yet been attributed to deficiency are likely to be so regarded in the future. Still other conditions within the field of psychiatry may, perhaps, be added to the list.

6. Any patient having neurologic or psychiatric symptoms such as are known to exist in deficiency states should be adequately treated in the early stages of the disorder when complete recovery of the nervous system may still be possible.

Note.—In order not to make this paper too long, I have omitted consideration of some important papers on the treatment of various neurologic lesions in man which have improved markedly after treatment with liver extract or with vitamin preparations.

Experimental work on animals has also given important results, but the response of animals to vitamin deficiencies differs in some respects from that of man.

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## THE RELATION OF HUMAN ENCEPHALITIS TO ENCEPHALOMYELITIS IN HORSES

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In 1931 Meyer, Haring and Howitt [1] reported the discovery of a virus as the cause of an epizootic of encephalomyelitis among horses and mules in the San Joaquin Valley of California during the summer of 1930. Since that time the disease has occurred in several Western and Midwestern states. Similar epizootics have occurred during the past seventy years, especially in the West Central states, but have been confused with other equine diseases. In 1933 the disease appeared in Maryland, Delaware, Virginia and New Jersey. In this year Ten Broeck and Merrill [2] and Giltner and Shahan [3] reported the isolation of an eastern strain of virus of equine encephalomyelitis which, though similar to the western strain, differed serologically. The disease in the horse was more acute and fatal, and the virus appeared to be more virulent for laboratory animals.

The viruses of equine encephalomyelitis differ immunologically from the viruses of lymphocytic choriomeningitis, the St. Louis type of encephalitis, Borna disease, vesicular stomatitis and poliomyelitis.[4]

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1. Meyer, K. F.; Haring, C. M., and Howitt, B. F.: The Etiology of Epizootic Encephalomyelitis of Horses in the San Joaquin Valley 1930, Science 74:227 (Aug. 28) 1931.

2. TenBroeck, Carl, and Merrill, M. H.: A Serological Difference Between Eastern and Western Equine Encephalomyelitis Virus, Proc. Soc. Exper. Biol. & Med. 31:217 (Nov.) 1933.

3. Giltner, L. T., and Shahan, M. S.: The 1933 Outbreak of Equine Encephalomyelitis in the Eastern States, North Am. Vet. 14:25 (Nov.) 1933.

4. Howitt, Beatrice F.: The Complement Fixation Reaction in Experimental Equine Encephalomyelitis, Lymphocytic Choriomeningitis, and the St. Louis Type of Encephalitis, J. Immunol. 33:235 (Sept.) 1937; Cross Immunization Experiments with Poliomyelitis Virus and That of Encephalomyelitis in Horses, Proc. Soc. Exper. Biol. & Med. 29:118 (Nov.) 1931. Cox, H. R., and Fite, G. L.: Serological Distinction Between the Virus of Encephalitis in St. Louis, 1933 Equine Encephalomyelitis and Vesicular Stomatitis, ibid. 31:499 (Jan.) 1934.

Present epidemiologic and experimental evidence points to the spread of infection by an insect vector rather than by contact. Experimentally mosquitoes can be infected and transmit the virus to laboratory animals and horses. Aedes aegypti, A. sollicitans, A. nigromaculis, A. dorsalis, A. albopictus Skuze, A. vexans and A. taeniorhynchus can transmit the western strain, A. cantator and A. sollicitans the eastern strain.[5] To date no one has found infected mosquitoes in localities where equine encephalomyelitis is prevalent.

Meyer [6] in 1932 suggested the possibility of human infection. He briefly reported three cases of encephalitis occurring in men closely associated with horses having encephalomyelitis. One, a ranch hand, died in July 1931; microscopic examination of the central nervous system showed manifestations resembling those in horses. A nonfatal case occurred in September 1931. Meyer was unable to demonstrate neutralization of the virus of equine encephalomyelitis by blood serum obtained during convalescence. A third case with recovery occurred in a veterinarian in July 1932. An attempt to isolate virus from the blood and spinal fluid was unsuccessful. This patient was given serum intramuscularly from a hyperimmunized horse.[7] He presented these cases with the suggestion that in the future the central nervous system of patients who died of atypical human encephalitis be investigated for the presence of the virus of equine encephalomyelitis.

Equine encephalitis has been definitely known to occur in Minnesota since the summer of 1934 and was very prevalent in Minnesota during the summer of 1937. Of 737,000 horses in Minnesota, 41,159 were affected and 9,200 of these died.[7] The western strain of encephalomyelitis virus is the only one that has been isolated in Minnesota.[8] Of the mosquitoes shown to transmit the western strain experimentally, three occur in Minnesota: A. vexans, A. nigromaculis and A. dorsalis.[9] A. vexans is one of the most common and widespread mosquitoes in Minnesota. It has been found as late as October. The other two mosquitoes are found in small numbers only. A. dorsalis has been found as late as July 27 and A. nigromaculis as late as August 4, but their times of occurrence have been incompletely studied.

During the last week of August and the first two weeks of September 1937 six cases of human encephalitis were reported from a county in northwestern Minnesota.[10] All were in farmers, five of whom had had contact with sick horses. The sixth patient (C. S.)

5. Kelser, R. A.: Mosquitoes as Vector of the Virus of Equine Encephalomyelitis, J. Am. Vet. M. A. 82:767 (May) 1933; Transmission of the Viruses of Equine Encephalomyelitis by Aedes Taeniorhynchus, Science 88:178 (Feb. 12) 1937. Merrill, M. H.; Lacaillade, C. W., and Ten Broeck, Carl: Mosquito Transmission of Equine Encephalomyelitis, ibid. 80:251 (Sept. 14) 1934. Madsen, D. E., and Knowlton, G. F.: Mosquito Transmission of Equine Encephalomyelitis, J. Am. Vet. M. A. 86:662, 1935. Simmons, J. S.; Reynolds, F. H. K., and Cornell, V. H.: Transmission of the Virus of Equine Encephalomyelitis Through Aedes Albopictus Skuze, Am. J. Trop. Med. 16:289 (May) 1936.

6. Meyer, K. F.: A Summary of Recent Studies in Equine Encephalomyelitis, Ann. Int. Med. 6:645 (Nov.) 1932; Equine Encephalomyelitis, North Am. Vet. 14:30 (June) 1933.

7. Cotton, C. E., executive secretary Minnesota State Live Stock Sanitary Board: Personal communication to the authors.

8. Howitt, Beatrice F.: An Immunological Study in Laboratory Animals of Thirteen Different Strains of Equine Encephalomyelitis, J. Immunol. 29:319 (Oct.) 1935. Fenstermacher, R., assistant professor of veterinary medicine, University of Minnesota: Personal communication to the authors.

9. Owen, W. B.: The Mosquitoes of Minnesota with Special Reference to Their Biology, Technical Bulletin 126, University of Minnesota Agricultural Experiment Station, November 1937.

10. In eleven counties in northwestern Minnesota, including the district in which human cases occurred, of 14,929 horses 3,826 horses were sick and 904 died. A. vexans and A. dorsalis have been found in this area.

had had no contact with sick horses at the time of onset of his illness. He had run a tractor on a farm in North Dakota not far from the Minnesota border. There was much equine encephalomyelitis in this locality. Two of the men had had contact with each other and with the same sick horses while threshing. The onset of their illnesses were August 29 and September 10. The others had not had any contact with one another or with any sick person. No other case occurred in the families of these six men.

All six patients were men ranging in age from 22 to 51. The onset of the disease was sudden with headache, nausea, vomiting, dizziness, drowsiness and fever. Two of the men died after illnesses of four and five days. In three cases the acute illness lasted about a week. In the sixth case (C. S.) the acute illness lasted about three weeks. An autopsy was done in one instance.

On microscopic examination of the central nervous system the chief pathologic changes were found in the gray matter of the spinal cord. On hematoxylin-eosin stain, about one third of the nerve cells in the cervical segment appeared to be affected. The cells were in various stages of disintegration. In the main they showed swelling and chromatolysis. Occasionally there was pyknosis and rarely slight evidence of neuronophagia. Scattered rather densely throughout the gray matter were nests of lymphocytes, consisting of from five to 100 cells. There were no definite hemorrhages. The white matter of the cord showed a mild degree of lymphocytic perivascular cuffing. Rarely there could be seen a small nest of glial cells numbering from five to twenty-five. The meninges showed a moderate degree of lymphocytic infiltration. Sections of the brain on hematoxylin-eosin stain showed minimal changes, which consisted mainly of a moderate degree of lymphocytic cuffing. There was no definite evidence of nerve cell degeneration and there were no distinct hemorrhages.

Blood was collected from three of the patients who recovered during January 1938 and the serums were forwarded to Dr. Carl Ten Broeck of the Rockefeller Institute for Medical Research. Under date of April 21, 1938, Dr. Ten Broeck reported that he had demonstrated neutralization of the western strain of equine encephalomyelitis virus by the serum of one of the patients (C. S.). Blood was collected again in May from this patient and neutralization was again demonstrated by Dr. Ten Broeck.

During the latter part of August and the early part of September of this year attacks of what appear to be a similar illness have occurred. Most of the patients have had no contact with sick horses. The majority live on farms or in small towns. Blood serums from patients have been collected for studies of the virus.

SUMMARY

In the summer of 1937 six cases of encephalitis occurred among farmers in localities where equine encephalomyelitis was prevalent. The blood serum of one of three patients was shown to neutralize the western strain of equine encephalomyelitis by Dr. Ten Broeck of the Rockefeller Institute for Medical Research.

As far as is known, this is the first time that neutralization of the virus of equine encephalomyelitis by human serum has been found.

## HUMAN ENCEPHALITIS

### EIGHT FATAL CASES, WITH FOUR DUE TO THE VIRUS OF EQUINE ENCEPHALOMYELITIS

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During the first week in August 1938 an outbreak of equine encephalomyelitis causing the death of more than 200 horses occurred in southeastern Massachusetts and Rhode Island. August 12 a girl aged 12 years was referred to the Haynes Memorial Hospital with a diagnosis of epidemic cerebrospinal meningitis. On admission a provisional diagnosis of encephalitis was made. Seven hours after admission the patient suddenly died. At autopsy the diagnosis of encephalitis was confirmed. No virus studies were made on the brain. Seventeen days later, August 29, a boy aged 13 years was admitted from the same city, presenting much the same clinical picture. In view of the existing epidemic of equine encephalomyelitis in the same area, the spinal fluid obtained from the lumbar puncture was injected into mice but the results were inconclusive. Death occurred twenty hours after entry. Unfortunately permission for an autopsy was not granted.

Similar cases continued to appear and were admitted to other hospitals, twenty-four cases in all to date. Six more patients with encephalitis were admitted to the Haynes Memorial Hospital up to September 17, all of whom died, and all were examined post mortem. Specimens of brain tissue collected in glycerin were sent to Dr. Fothergill at the Boston Children's Hospital and through the state department of health to Dr. L. T. Webster at the Rockefeller Institute. September 13 Dr. Fothergill found the virus of the eastern strain of equine encephalomyelitis in a patient who had died at the Children's Hospital, the report of which was published in the *New England Journal of Medicine*.[1] September 15 Dr. Webster reported that he had recovered this same strain of virus from three of our patients and later from a fourth. He has since published his observations on these and four other cases.[2]

The high mortality rate among the horses has been paralleled in these human cases. Furthermore, it is of epidemiologic interest that the peak of the human cases of encephalitis in this area appears to have coincided with the peak of the epidemic in the horses. None of our patients came in contact with a horse but they all had been living within the area where horses had been stricken. Simmons [3] has recently discussed the role of mosquitoes in the transmission of the virus among horses. The fact that in this region seven established cases of this equine type should have occurred in human beings during a period when mosquitoes were unusually

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Dr. Leß. D. Fothergill and Dr. Sidney Farber of the Children's Hospital, Dr. L. T. Webster of the Rockefeller Institute and Dr. R. F. Feemster of the Massachusetts State Department of Health gave their cooperation and assistance in the study of these cases.

1. Fothergill, L. D.; Dingle, J. H.; Farber, Sidney, and Connerley, M. L.: Human Encephalitis Caused by the Virus of the Eastern Variety of Equine Encephalomyelitis, New England J. Med. 219: 411 (Sept. 22) 1938.

2. Webster, L. T., and Wright, F. H.: Recovery of Eastern Equine Encephalomyelitis Virus from Brain Tissue of Human Cases of Encephalitis in Massachusetts, Science 88: 305 (Sept. 30) 1938.

3. Simmons, J. S.: The United States Army's War in the Air Against the Mosquito-Borne Diseases, Am. J. M. Sc. 196: 165-166 (Aug.) 1938.

prevalent prompts us to report the clinical aspects and pathologic changes found in eight fatal cases of encephalitis from this area which came under our observation at the Haynes Memorial Hospital, in four of which this virulent equine strain has been found.

The clinical aspect of these Massachusetts cases differs from epidemic human encephalitis in the much greater severity of the symptoms and the high mortality. In the St. Louis epidemic[4] the incidence and the mortality rate were definitely greater in older persons, yet it appears from the few reported human cases of encephalitis in this minor epidemic that children are more susceptible than adults. The question arises as to whether there have been milder cases in which recovery has occurred. That is a problem outside the scope of this paper. Of course a great number of mild cases of encephalitis go unrecognized as such. This is certainly true of the milder forms of encephalitis accompanying chickenpox, the meningo-encephalitis of mumps and measles, and even encephalitis lethargica. It seems, therefore, reasonable to suppose that some cases have passed unrecognized, a factor which if known would modify the case rate mortality. However, it is of significance that very few horses recovered and that the only human subjects as yet positively known to have harbored this virulent strain of equine virus are dead.

The variation in the onset is particularly striking. The onset in the infants was abrupt; in the three older children and the adult the period of invasion lasted several days before the signs of encephalitis set in. Patient 6 had complained of pain in the back of the legs for two weeks before admission to the hospital. In cases 2 and 8 there was a period of remission with definite improvement in the symptoms. In all the cases there seemed to be an abruptness in the onset of the severer symptoms in the form of dizziness, vomiting, drowsiness, twitching of the muscles or convulsions. Aphasia, diplopia and palsies signified cerebral insults. Hyperpyrexia was constant. All the symptoms proceeded to a lethargy and coma. The deaths were all due to encephalitis, and the terminal evidence of myocardial insufficiency and pulmonary symptoms contributed little or not at all as actual causes of death. This again is in striking contrast to the St. Louis epidemic, where not more than 10 per cent of the deaths were attributable to uncomplicated epidemic encephalitis.[4]

This statement requires qualification because a remarkable complication did exist in three of the four infants (cases 4, 5 and 7), namely whooping cough; in each one a diagnosis from the cough had been made three weeks before the onset of the symptoms of encephalitis, prior to which they had shown an improvement in the cough. All three of these were referred to the hospital as having "whooping cough with convulsions." However, they all showed signs and symptoms of a severe encephalitis, which was confirmed by the appearance of the brain at autopsy and by subsequent microscopic appearances, all of which were entirely out of keeping with those seen in whooping cough. In two of these cases the virus of the eastern strain of equine encephalomyelitis was found in the brain tissue. It was the severe type of encephalitis resembling that observed in the other cases and the appearance of the brain at autopsy that prompted us to suspect that we were dealing with something more than the cerebral complications of whooping cough.

4. Burr, D. P.: The Encephalitis Epidemic in St. Louis, Ann. Int. Med. 8:37 (July) 1934.

A contagious disease service receives numerous cases of convulsions occurring in the course of whooping cough. Convulsions occurred in 2.3 per cent of cases of pertussis at the Metropolitan Asylums Board Hospitals in London,[5] 2.2 per cent at the Herman Kiefer Hospital in Detroit[6] and in 7.4 per cent of our cases at the Haynes Memorial Hospital. Just what the percentage of this complication is in this disease remains unknown, because only comparatively few patients with uncomplicated pertussis are hospitalized. The spinal fluid in pertussis without neurologic complications is normal.[7] Ordinarily when convulsions occur in this disease the spinal fluid shows only a moderate increase in the number of cells, from 10 to 100, although an accompanying meningitis shows a turbid fluid with a cell count in the thousands.[8] The white blood count may often rise to over 100,000 in severe whooping cough in infants, and the peak is reached when convulsions take place. A relative lymphocytosis prevails unless a mixed infection occurs with bronchopneumonia or otitis media.

Encephalitis[9] is a very rare complication of whooping cough and, if recovery takes place, is apt to leave a wake of mental disorders. Esche[10] reports only one case among 172 cerebral complications. Sears[11] has suggested that a special neurotropic virus might be stimulated to activity by the pertussis, as has been considered in the case of the encephalitis following acute exanthematous diseases and vaccination, in which this complication also appears after the acute phase has passed. Furthermore, Sears points out that the encephalitis of whooping cough cannot be differentiated from that which occurs in the course of other acute infections. Many writers on the subject are coming more and more to the opinion that a mechanical factor alone does not account for the many neurologic conditions which can take place in pertussis.

Reports are extremely rare of the clinical manifestations of encephalitis in the course of pertussis. In one case reported from Buenos Aires[12] the cell count of the spinal fluid was 70 and all were polymorphonuclear leukocytes. In a case reported from Germany[13] in which recovery occurred the white count was 61,000 with 71 per cent lymphocytes, while the spinal fluid was clear with only 12 cells.

It is therefore reasonable to assume from the severity of the clinical course, from the gross appearance at autopsy and from the histologic specimens as well as from the finding of the virus in the brains of two of these infants that all three suffering from whooping cough died of an encephalitis due to the virus of the eastern strain of equine encephalomyelitis.

## REPORT OF CASES

CASE 1.—A girl aged 12 years, from Brockton, had had chickenpox and measles. The tonsils and adenoids had been removed. Otherwise the patient had always been well. The

5. Rolleston, J. D.: Acute Infectious Diseases, New York, Physicians & Surgeons Book Company, 1925, p. 115.
6. Gordon, J. E.: Herman Kiefer Hospital Five Year Report, 1927-1931, p. 377.
7. Magnussen, J. H.: Findings of Cerebrospinal Fluid in Pertussis Without Neurological Complications, Acta pediat. 20:222, 1937.
8. Reiche, F.: Keuchhustenkrämpfe, Ztschr. f. Kinderh. 58:34, 1930.
9. Milnlowski, W.: Ueber encephalitische Erkrankungen bei Keuchhusten, Acta pediat. 9:454, 1930. Elsy, R. C.: Neurological Complications of Whooping Cough, New England J. Med. 202:165 (July 24) 1930. Comby, Jules, and Comby, Marie-Thérèse: L'encéphalite aigue au cours de la coqueluche, Arch. de méd. d. enf. 38:597 (Oct.) 1935.
10. Esche, C.: Pathogenese der cerebralen Komplikationen des Keuchhustens, Monatschr. f. Kinderh. 61:439, 1935.
11. Sears, W. G.: Nervous Complications of Whooping Cough, Brit. J. Child. Dis. 26:191 (July-Sept.) 1929.
12. Mendilaharsu, J. E., and Calcerdas, J. M.: Encefalopatias coqueluchosas, Semana méd. 1:29 (Jan. 7) 1937.
13. Wiesner, Bernhard: Eine tödlich blodige Variolaform der Keuchhusten-Encephalitis, München. med. Wchnschr. 82:786 (May 16) 1935.

father died of rheumatic fever with endocarditis. She had a sister with rheumatic heart disease.

Onset occurred Aug. 2, 1938, with severe frontal headache, nausea without vomiting, and increasing drowsiness. August 9 there had been such an improvement in these symptoms that she went to the theater. That evening these symptoms reappeared and grew gradually more severe. On the 11th vomiting began and she complained of pain in the back of the neck. The following day there was intermittent twitching of both shoulders. She was admitted to the Brockton Hospital with pain in the right ear, tinnitus, dizziness, rigidity of neck and nystagmus of the right eye. The temperature was 104.6 F., the pulse 130 and the respiratory rate 25. Lumbar puncture revealed a hazy cerebrospinal fluid with an initial pressure of 320. The cell count was 920, mostly polymorphonuclear leukocytes with a few red cells. Prontosil (the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3', 6' disulfonic acid) was given intramuscularly.

August 12 she was referred to the Haynes Memorial Hospital with a diagnosis of epidemic cerebrospinal meningitis. There was deep stupor on admission. The temperature was 102.6 F., pulse 100 and respiratory rate 26. The pupils were equal and moderately dilated, with a sluggish reaction to light. There was no nystagmus or strabismus. Muscular twitchings were present over the mandibles. There was involuntary urination (prontosil-colored urine). The lungs were normal. The size and position of the heart were normal but there was a gallop rhythm with a systolic murmur at the apex transmitted to the axilla. The abdomen was normal. Reflex of the biceps and triceps and the knee jerk were absent. The Kernig and Babinski reflexes were bilateral. The hemoglobin content was 90 per cent. The white blood cells numbered 19,050, with 90 per cent polymorphonuclear leukocytes. Examination of the cerebrospinal fluid revealed a normal pressure, a cell count of 1,500, polymorphonuclear leukocytes predominating; tubercle bacilli were not present. The patient suddenly became cyanotic and died at 8:15 p. m.

The family history and cardiac murmur bring up consideration of cerebral embolus, but at autopsy the heart was entirely normal. Furthermore, there was nothing sudden about the onset. Clinically this was a remittent type of encephalitis, the second phase being very severe and ending abruptly with simultaneous cessation of respiration and heart beat. No virus studies were made. Death occurred on the tenth day of the disease.

CASE 2.—A boy aged 13 years, from Brockton, with a negative past history, complained of frontal headache, dizziness and weakness August 22, which caused him to remain in bed. The following two days he was up and about, with intermittent headache, anorexia and backache. August 25 he stayed in bed because of weakness, headache, backache and pains in the legs. On the 27th there were drowsiness and photophobia. On the 28th the patient vomited and had a convulsion; he was taken to the Brockton Hospital, where he showed twitching of a generalized nature, rigidity of the neck with hyperextension and stupor, from which he could be aroused to answer questions. The pupils were equal and reacted to light. The fundi showed clear disks. The tendon reflexes in the arms were absent, in the legs they were diminished. The Kernig and Babinski reflexes were marked on both sides. Examination of the urine was essentially negative. The hemoglobin content was 100 per cent; red blood cells numbered 5,280,000, white blood cells 18,400: polymorphonuclears 81 per cent, lymphocytes 14 per cent, monocytes 5 per cent, platelets normal. Lumbar puncture revealed: initial pressure 250; dynamics normal; cerebrospinal fluid hazy, with a cell count of 990, mostly polymorphonuclears, sugar 83 mg. per hundred cubic centimeters and globulin positive. Two hours after entry facial palsy developed on the left side. He was referred to the Haynes Memorial Hospital August 29 with a diagnosis of poliomyelitis, encephalitis or lymphocytic meningitis. On admission the temperature was 104.6 F., the pulse rate 110 and the respiration shallow, at the rate of 36. Hyperesthesia was present on the anterior half of the scalp. The pupils were equal and reacted to light. There was slight ptosis of the left eyelid with left facial paralysis. The jaws were firmly set. There was marked rigidity of the neck with hyperextension and marked twitchings of the arms and shoulders. The lungs were normal. The size and position of the heart were normal; there was a marked systolic murmur over the precordia, loudest at the base. The abdomen was normal. Tendon reflexes of the arms and legs were absent. Ankle clonus was absent. The Kernig and Babinski reflexes were present on both sides. Examinations of the blood and spinal fluid gave essentially the same results as those reported from the Brockton Hospital. Four grains (0.26 Gm.) of soluble phenobarbital was given intravenously. August 30 at 7:30 a. m. a convulsion occurred, with rigidity and opisthotonos lasting several minutes. The injection of soluble phenobarbital was repeated and lumbar puncture was done again. At 9:30 a. m. the patient had a convulsion. Fifty cc. of 25 per cent dextrose was given intravenously. Coarse moist rales were heard throughout. At 11 o'clock there was less rigidity of the jaws and neck. Cyanosis was evident. At 1:15 p. m. the mouth was filled with frothy mucus. At 5 o'clock the patient was completely relaxed. Shallow rapid respiration set in and the patient died at 8:10 p. m.

This was a remittent type of encephalitis with facial paralysis, convulsions and opisthotonos. Virus studies were made on the spinal fluid with inconclusive results to date. Death occurred on the eighth day of disease; permission for autopsy was not given.

CASE 3.—A girl aged 13 months, who lived in Abington, had the onset of this illness August 29 with restlessness, irritability, anorexia, drowsiness, fever and vomiting. Convulsions occurred at 2 and 2:30 p. m. She was taken to the Moore Hospital in Brockton, where she was found to have rigidity of the neck and flaccid paralysis of the right arm and leg. On lumbar puncture the cerebrospinal fluid showed 1,500 cells, all lymphocytes. She had numerous mosquito bites. She was transferred to Haynes Memorial August 30 at 6:30 p. m. On admission the rectal temperature was 104.4 F., pulse rate 162 and respiratory rate 42. There was a puffy appearance about the eyes and of the hands. She did not resist examination but took fluid with difficulty. Examination of the nose and throat was negative. The lungs, heart and abdomen were normal. The pupils were equal and reacted to light. There was no evidence of paralysis of the cranial nerves or of the extremities. There was moderate rigidity of the neck. The tendon reflexes of the arms and legs were normal. The abdominal reflex was absent on the right. The Kernig and Babinski reflexes and ankle clonus were absent. The hemoglobin content was 85 per cent. Red blood cells numbered 4,400,000, white blood cells 27,250, with polymorphonuclear leukocytes 84 per cent and lymphocytes 13 per cent. The cerebrospinal fluid had the appearance of ground glass; it had a pressure of 240, and 525 cells. Polymorphonuclear leukocytes and lymphocytes were equal. August 31 muscular twitchings developed over the entire left side. The patient became lethargic. September 1 lumbar puncture showed a pressure of 135, and 660 cells with lymphocytes predominating. Vomiting and convulsions set in. September 2 the rectal temperature was 107 F., the pulse rate 160 and the respiratory rate 90. Convulsions continued, with general rigidity. Cistern puncture showed the cerebrospinal fluid clear, a pressure of 108 and cells 252, mostly lymphocytes. September 3 the rectal temperature was 103 F.; the patient was comatose and there was muscular twitching. Small petechial spots appeared on the anterior and posterior surfaces of both arms. The temperature, pulse rate and respiratory rate fell from here on. September 4 the white blood cells numbered 8,200, polymorphonuclear leukocytes 20 per cent, lymphocytes 75 per cent and endothelial phagocytes 5 per cent. September 6 the comatose condition continued with complete relaxation. September 7 lumbar puncture revealed a cell count of 150, mostly polymorphonucleara. There were fine moist rales at both bases. The patient died September 9. Intravenous dextrose and saline clyses were given throughout, along with feeding by nasal tube during the coma.

This was a case of encephalitis with convulsions on the day of onset, growing progressively worse, with temporary paralyses, muscular twitchings and rigidity

merging into relaxation. On the fifth day the rectal temperature reached 107 F., falling gradually to normal before death on the twelfth day. Results of studies on the virus showed that it was positive for the equine strain.

Case 4.—A boy aged 2 years 10 months had had measles at 3 months and chickenpox at 1 year. He had not been vaccinated. He lived in Plainfield and two days before the onset of the present illness was in Randolph and Brockton. He had had whooping cough for three weeks and was said to have been improving as regards frequency and severity of paroxysms. At the onset September 1 at noon he had a convulsion, which occurred when he was asleep. Dr. Farley found no meningeal signs. A second convulsion occurred at 3 p. m., after which there was rigidity of the neck and spine with generalized muscular twitchings and irregular respirations. He was admitted to the Haynes Memorial Hospital at 6 o'clock. He was well developed and well nourished. The rectal temperature was 101.2 F., the pulse rate 160 and respiratory rate 32. He was stuporous and rigid and could not be aroused. There were drooling and persistent twitchings about the mouth, rolling of the eyeballs and occasional convulsive movements of the left arm and leg. The teeth were clenched. The fauces was normal except for post nasal mucus. The left tympanum was injected. The skin was clear. There was no nasal discharge. The pupils were dilated and equal and reacted sluggishly to light; the eyeballs oscillated. The cervical glands were slightly palpable on both sides. The lungs, heart and abdomen were normal. There was rigidity of the neck and spine. The biceps reflex on the left side, the knee jerk reflex on both sides and the abdominal reflexes were absent. The cremasteric reflex was present but was sluggish on the right. The Brudzinski sign was present. The Kernig and Babinski signs and ankle clonus were absent. There was no evidence of paralysis. The white blood cells numbered 65,900; polymorphonuclear leukocytes 53 per cent, lymphocytes 43 per cent. On lumbar puncture pressure of the cerebrospinal fluid was 210 and showed cells 200, lymphocytes predominating, sugar 143 and globulin 95. There were infrequent paroxysms of coughing with whoop. September 2, the temperature was 104.4 F., the pulse rate 160 and respiratory rate 60. Convulsions continued, beginning in the right arm and then the right leg, with opisthotonos and cyanosis and cessation of respirations. The patient became comatose. The cremasteric reflex was absent. Lumbar puncture gave the same results. September 3 the temperature was 104.6 F., the pulse rate 160 and the respiratory rate 28, of Cheyne-Stokes type and stertorous. The patient died at 8 p. m. Treatment consisted of ½₀ grain (0.002 Gm.) of morphine, dextrose intravenously and saline solution by hypodermoclysis, and repeated artificial respiration.

In this case encephalitis was ushered in by convulsions three weeks after the onset of whooping cough. Muscular twitchings, opisthotonos, rigidity, cyanosis and respiratory failure occurred. Death transpired on the third day of the disease. The virus was positive for the equine strain.

Case 5.—A girl aged 13 months, who lived in Marlboro, had a negative past history. She had had a cough for three weeks, which was diagnosed by a local physician as whooping cough; it was mild and was improving. Except for the cough she was well. The onset of the present acute condition took place September 1 with a temperature of 105 F., projectile vomiting and diarrhea, and she was seen again by her physician. On the morning of September 3 she became lethargic and convulsive movements of the face and arms developed. She was referred from the Children's Hospital because of whooping cough and admitted to the Haynes Memorial Hospital at 3 p. m. The rectal temperature was 102.6 F., the heart rate 180, and the respiratory rate 28. The patient was well developed and well nourished and had moderate rigidity of the neck and spine; the head was turned persistently to the left, and the eyes were wide open and rolled upward and to the left with lateral nystagmus and diminished wink reflex. The pupils were equal and reacted to light. There was occasional muscular twitching of the limbs and about the mouth. The right tympanum was slightly injected. The teeth were clenched. The gag reflex was present. The pharynx was injected and the tonsils were slightly enlarged. There was coughing without whoop. There was slight cervical adenopathy on the left. The lungs, heart and abdomen were normal. The arms were flexed and spastic. The biceps and triceps reflexes were normal. The legs were extended, rigid and spastic. The knee jerks were increased, on the right more so than on the left. The Kernig sign was present on both sides and the Babinski sign on the right; ankle clonus was absent. Tâche cérébrale was absent. The white blood cell count was 50,900, with polymorphonuclear leukocytes 83 per cent. On lumbar puncture the cerebrospinal fluid had a ground glass appearance, with a pressure of 240, cell count of 710 with polymorphonuclears 56 per cent. Globulin and sugar were normal. During the evening convulsions lasted one hour; the face, arms and legs twitched constantly, followed by shallow respirations and complete relaxation. The patient vomited. The rectal temperature rose to 108.5 F. and she died with respiratory failure at 1:35 p. m. September 4.

In this case encephalitis was ushered in by projectile vomiting and diarrhea, occurring three weeks after the onset of whooping cough. The diarrhea stopped after the first day. Convulsions, muscular twitchings and spasticity were predominant symptoms. Death occurred on the fourth day. The virus was positive for the equine strain.

Case 6.—A girl aged 10 years, who lived in Canton, had measles at 2, was vaccinated at 5 and had a tonsillectomy and adenoidectomy in May 1938.

The patient was well until August 22, when she began to complain of persisting pain in the back of the legs. September 4 headache, stiffness of the neck, drowsiness, fever and vomiting developed. Her parents noticed that she talked from the corners of her mouth. She then became stuporous and the next day was admitted to the Norwood Hospital, where a lumbar puncture was done which showed 814 cells, mostly polymorphonuclears, and slightly increased globulin. Prontosil was administered. The patient was transferred to the Haynes Memorial Hospital at noon with a temperature of 104.4 F., pulse rate 120, and respiratory rate 24. She was well developed and well nourished. There was rigidity of the neck and spine and she was lethargic, uncooperative and unresponsive. The skin had a normal appearance. The pupils were equal and reacted to light; the fundi were normal; there was no nystagmus or palsy; the wink reflex was active. The ears were normal. There was no nasal discharge. The pharynx was slightly injected. There were no tonsils. The gag reflex was present. The lungs were normal. The size and position of the heart were normal with a soft systolic murmur, loudest just above the apex. The abdomen was normal. The biceps and triceps reflexes were barely perceptible. The abdominal reflexes were absent. The knee jerks were active, on the right more so than on the left. The Babinski sign was present, bilateral and contralateral on the right leg. The Brudzinski sign was present on the left. The white blood cells numbered 27,550 with neutrophils 80 per cent. Lumbar puncture showed the cerebrospinal fluid to have a pressure of 200, a ground glass appearance, a cell count of 1,205, 61 per cent being polymorphonuclears; protein 83, sugar 72. September 6 the lethargic condition continued; the patient could not be aroused. She was totally relaxed but at times the neck would become rigid. Lumbar puncture was repeated; 14 cc. of cerebrospinal fluid was removed and showed 950 cells. The white blood cell count was 11,350: neutrophils 68 per cent, lymphocytes 28 per cent, endothelial phagocytes 4 per cent. The patient continued to swallow normally. The temperature rose to 108 F., and she died at 4:25 p. m. Treatment had consisted of prontosil and intravenous dextrose.

In this case of encephalitis there were pains in the back of the legs for two weeks before onset of headache, drowsiness, rigidity of the neck and vomiting,

which proceeded to coma and a temperature of 108 F. There were no tremors or muscular twitchings. Death occurred on the sixteenth day of the disease. The virus was positive for the equine strain.

CASE 7.—A boy aged 10 months, living in Randolph, had a negative past history. Whooping cough developed on August 23. Although the paroxysms of typical whooping cough persisted, improvement was noted. He had occasionally lost a meal with the coughing but on the whole had retained his feedings well. The bowels moved normally. September 14 there was no bowel movement and toward evening he became very irritable. Marked sweating and blueness of the arms were noted. There was no muscular twitching or convulsions. He was admitted to the Haynes Memorial Hospital September 15 at 2 p. m. with a temperature of 107.2 F. On examination the baby was well developed and well nourished, was in a stuporous condition and yet responded to stimuli. There was rigidity of the neck. The skin showed a mottled lividity of the limbs and body with general cyanosis. There were staring and vertical nystagmus; the pupils were equal and contracted but reacted to light. The ears, throat and nose were normal. The tongue was dry. Respirations were labored with grunting. There were moist rales throughout the chest but no dulness. The heart was regular, too rapid to count; no murmurs were heard. The abdomen was normal. Knee jerk, abdominal and cremasteric reflexes were absent. The Kernig sign and ankle clonus were absent. No muscular tremors, twitchings or paralyses were noted. The white blood cells numbered 94,500, with neutrophils 27 per cent, lymphocytes 66 per cent, endothelial phagocytes 3 per cent and myelocytes 4 per cent. The red blood cells numbered 6,100,000. Lumbar puncture showed the cerebrospinal fluid to be clear, with a pressure of 108, cells 7, all lymphocytes, globulin was normal, sugar increased. The patient died at 5:25 p. m.

In this case of encephalitis in an infant, occurring at the end of the third week of whooping cough, onset occurred with sudden fever, sweating, irritability followed by lethargy, cyanosis, rigidity of the neck and nystagmus. Tremors, twitching and convulsions were absent. The patient died within twenty-four hours of the onset. Autopsy showed early signs of encephalitis. Results of studies of the virus were negative for the equine strain. Of course, this may be a straight case of pertussis encephalitis, but it occurred within the area of the equine cases, and other infants from this area, proved to have died of this equine virus at other Boston hospitals, have shown similar symptoms and changes in the spinal fluid at the onset, with subsequent changes on the second day similar to those found in our other cases. Consequently, we feel justified in assuming that this patient died before the full picture was established, a phenomenon comparable to the purpura variolosa of smallpox.

CASE 8.—A man aged 50, a shoemaker, on the WPA for two years, who lived in Brockton, had a negative past history. September 12 headache, fever and tremors of the left hand developed. These symptoms improved until September 16. Early on the morning of the 17th a tonic muscle spasm occurred in the right hand and left leg, with complete aphasia. He was taken to the Brockton Hospital and transferred immediately to the Haynes Memorial Hospital. On admission the temperature was 101 F., the pulse rate 104, and the respiratory rate 30. He was well developed and stocky. He was very drowsy but could be aroused. The skin had a normal appearance. There was staring and the eyes rolled outward. The pupils were equal and widely dilated and reacted to light. Corneal reflexes were present. The fundi showed pale disks. The retinas were congested. There were no hemorrhages or tortuosity. The ears were normal. There was no nasal discharge. The jaws were rigid. The fauces was not seen. Respiration was shallow. There were a few coarse rales at the base of the right lung. The size and position of the heart were normal and the sounds were distant but clear. The blood pressure was 150 systolic, 90 diastolic. The abdomen and genitalia were normal. The extremities showed no edema or lesions. There was marked rigidity of the neck. There was facial palsy on the right side. Flaccid paralysis of the left arm and left leg was present. Tendon reflexes revealed the left biceps greater than the right. Knee jerks were equal and hyperactive. The abdominal and cremasteric reflexes were absent on the left. There was a bilateral Kernig sign and a slight Babinski sign on the left. The right plantar reflex was normal. The Oppenheim, Chaddock and Gordon signs were absent. Ankle clonus was absent. Micturition was involuntary. Urinalysis showed acidity, a large trace of albumin, sugar, a trace of ketone and no bile; the sediment showed an occasional leukocyte and many granular casts. Red blood cells numbered 4,500,000; white blood cells 15,950: neutrophils 89 per cent, lymphocytes 5 per cent and endothelial phagocytes 6 per cent. Chemical analysis of the blood revealed nonprotein nitrogen 50, uric acid 6.1, sugar 154. The Wassermann and Kahn reactions of the blood were negative. The colloidal gold curve was 00012,21000. On lumbar puncture the cerebrospinal fluid gave the appearance of ground glass and had a pressure of 250 and a cell count of 875, with 72 per cent polymorphonuclears. Sugar was normal and globulin was increased.

September 18 the temperature was 104 F., the pulse rate 130, and the respiratory rate 38. On lumbar puncture the pressure of the cerebrospinal fluid was 210 and the cell count was 300: red blood cells 100, white blood cells 200, of which 80 per cent were lymphocytes. The bowels moved naturally. There were a few scattered rales over the back. The clinical diagnoses offered by three members of the staff were (1) cerebral thrombosis with encephalitis, (2) encephalitis with cerebral hemorrhage and (3) cerebral accident.

September 19 the temperature was 100.4 F., the pulse rate 130 and the respiratory rate 30. The patient was more conscious. There was profuse sweating. There were marked tremors of the face, left hand and leg. There was a tremor of the tongue. The pupils were active and equal. The knee jerks were hyperactive and equal. The Babinski, Gordon and Oppenheim signs were absent. The cremasteric reflex was bilateral. The abdominal reflexes were absent. There was marked rigidity of the neck. Aphasia persisted. Fluids could be taken. The blood pressure was 130 systolic, 100 diastolic. White blood cells numbered 17,500: neutrophils 89 per cent, lymphocytes 7 per cent and endothelial phagocytes 4 per cent.

September 20 the temperature was 100 F., pulse rate 120, respiratory rate 30. The patient was even more conscious than the day before. Aphasia persisted. He took fluids well and slept most of the time. Chemical analysis of the blood revealed nonprotein nitrogen 67, urea nitrogen 43, uric acid 6.1, sugar 154. On lumbar puncture the cerebrospinal fluid was clear, with a pressure of 182, a cell count of 100, 94 per cent being lymphocytes and a few red blood cells.

September 21 the temperature was 103 F., pulse rate 140, respiratory rate 60. The patient was in a semicomatose condition. There were numerous moist rales throughout. The clinical diagnosis of the entire staff was eastern strain of equine encephalitis. Daily urinalyses gave the same results as on admission. Chemical analysis of the blood showed nonprotein nitrogen 75, sugar 154. The patient died at 5:40 p. m.

In this case there was gradual onset of encephalitis with remission. Muscle spasm and aphasia developed on the fourth day. There was contralateral flaccid paralysis of the face, arm and leg. Death occurred on the tenth day of the disease. There was a delay of twelve hours in obtaining permission for the autopsy, which may well be the cause of not finding the virus in the brain tissue. In horses it is well known that in order to recover the virus one must place specimens of the brain in 50 per cent neutral glycerin solution immediately after death. Indeed, best results are obtained by veterinarians when the afflicted horse is killed and the brain examined before decomposition sets in.

### PATHOLOGY

The brains obtained from patients in this epidemic presented lesions much more acute than any we had previously observed in the several types of encephalitis encountered at the Haynes Memorial Hospital. The disease with which we are dealing is certainly not of the Economo, postinfectious or postvaccinal type and can be easily differentiated from them histologically. It corresponds roughly to the picture observed in the St. Louis, Japanese and Winnipeg epidemics, though more severe. The seven cases which came to necropsy consisted of four infants, two children and one adult.

The abdominal and thoracic viscera and associated tissues presented essentially the same gross and microscopic changes, namely a marked general hyperemia, varying degrees of anasarca, slight toxic changes in the liver and kidneys, and a well defined toxic lymphadenopathy and splenitis. The three cases of pertussis showed somewhat divergent pulmonary changes. Case 5 presented the least possible pulmonary edema. A moderate acute bronchitis and early interstitial pneumonitis was present in case 7, while case 4 showed only a mild chronic bronchitis in keeping with the terminal phase of pertussis and an early interstitial pneumonitis. Unfortunately the adult was not examined until twelve hours after death and showed marked postmortem degeneration. Nevertheless, definite vascular engorgement and moderate senile changes were demonstrable. In view of the marked hyperpyrexia in most of the cases, it is perhaps remarkable that more extensive visceral changes were not encountered.

The macroscopic appearance of the brains was strikingly similar but nonspecific. The vessels of the pia arachnoid were markedly engorged, the finer capillaries standing out as a delicate bright red network. The intensity of vascular engorgement increased from above downward, so that about the brain stem one had to look sharply to be sure there was no actual extravasation of blood. The membranes of the cervical cord showed a definite, though not abrupt, transition from the fiery red of the pons and medulla to a degree of congestion more consistent with the upper surface of the hemispheres. No compression rings were observed. The subarachnoid space usually contained a small amount of slightly turbid, watery fluid in which no frank pus or fibrin could be demonstrated macroscopically. On section the brains were universally softer than normal, this being directly proportional to the degree of histologic involvement. The cut surfaces were varying shades of light to dark salmon pink, against which the engorged vessels stood out prominently. No gross petechiae or thrombi could be demonstrated. The ventricles were consistently normal, containing a small amount of clear fluid and presenting an ependymal surface which was not remarkable. There was no evidence of obstruction to the aqueducts.

Examination of sections from various levels of the central nervous system showed essentially the same microscopic changes. As the congestion and perivascular lesions increased in intensity from the cortex to the brain stem, so the acute disseminate encephalomyelitis reached its maximum intensity of destruction in the basal ganglions, pons and medulla. No part of the brain studied was consistently free from pathologic changes. At present we are unable to correlate the degree of microscopic damage present with the duration of the disease. More comprehensive neuropathologic studies are being undertaken and will be reported later. At present one may say that cases 1, 3 and 8, each of approximately ten days' duration, presented the most severe lesions, while case 6, of sixteen days' duration, showed only moderate changes. Case 7, of twenty-four hours' duration, presented little more than congestive and edematous phenomena.

The subarachnoid space in all instances contained much serofibrinous coagulum, in the meshes of which were large numbers of lymphocytes, monocytes and neutrophils. The cells varied in proportion at various sites, but in general lymphocytes predominated. The blood vessels which penetrated the parenchyma all showed profound perivascular cuffing with lymphocytes, neutrophils, monocytes and rare plasma cells. Not only were the adventitial lymph spaces stuffed with such cells but they also invaded the surrounding brain tissue to some extent. Many of the Virchow-Robin spaces were filled with extravasated red blood cells, but otherwise only rare petechiae were encountered. The most striking vascular phenomenon in our cases was the frequent predominance of neutrophils in the perivascular accumulations. In addition, many arterial walls were so infiltrated with these cells that the lesion would have to be classified as an acute arteritis. Terminal fibrin thrombi were found in only rare capillaries. No bacteria could be demonstrated in relation to any lesions.

In the more severe cases, all layers of the cortex, basal ganglions, pons, medulla and parts of the cervical cord showed a marked diffuse infiltration with neutrophils, occasional lymphocytes and monocytes and also discrete and confluent areas of profound necrosis infiltrated with similar cells. Degenerations were found in the neurons and neuroglia of each case, but these were not uniform in degree or in distribution. In some instances the pyramidal layer of the cortex presented minute foci of cellular infiltration and glial nodules, but in general the degeneration in the parenchyma did not become extensive until one reached the ganglionic layer. The basal ganglions, pons and medulla presented widely divergent degeneration of the nucleus and tract, scarcely any two of which were similar. In general the median lemniscus, transverse fibers and pontile nuclei suffered heavily, while only occasional lesions of the olivary nucleus were noted. Many of the nuclei of the cranial nerves were involved. Both anterior and posterior horn cells of the cervical cord presented lesions, and the one complete cord examined (case 8) showed slight, but positive, involvement at all levels. Small focal lesions were noted in the molecular layer of the cerebellar hemispheres, but no foci were seen in the nuclear layer. It seems probable that further study may reveal lesions here. Occasional Purkinje cells were destroyed. The cellular degenerations were of virtually every conceivable type, from simple eccentricity and swelling of the nuclei to complete pyknosis, autolysis and neuronophagia. These changes were of course more marked in the cases of greatest severity. No inclusion bodies have been found in any of the sections so far examined.

### SUMMARY

Eight fatal human cases of acute encephalitis were observed. All the patients resided in an area where an epidemic of the eastern strain of equine encephalomyelitis involved more than 200 horses during the same period and where mosquitoes were unusually prevalent. Autopsies were performed in seven of these eight human cases, and in four the virus of the eastern strain of equine encephalomyelitis was recovered from the brain.

The clinical diagnosis of encephalitis was made in all cases before death, but by no means was this possible at the onset or until lethargy was pronounced. Hyperpyrexia was a predominant feature. The onset was abrupt in the four infants and more gradual in the older patients, being remittent in two. The clinical course in the older patients was similar to that of the rare severe fulminating forms of human epidemic encephalitis. The clinical laboratory examinations showed wide variations. The blood showed a fairly constant tendency toward a pronounced polymorphonuclear leukocytosis as the disease progressed. The cerebrospinal fluid tended toward a high cell count, but there was no constancy in the predominating cells. Three cases occurred in the course of whooping cough, in two of which the presence of this equine strain of virus was found. The finding of this virus in these two cases confirms the current hypothesis that encephalitis arising in the course of whooping cough can be the result of a superimposed infection.

The virus of the eastern strain of equine encephalomyelitis causes in human beings a profound, acute, disseminate and focal encephalomyelitis characterized by intense vascular engorgement, perivascular and parenchymatous cellular infiltration and extreme degenerative changes in the nerve cells. The gross pathologic manifestations are not specific. In the severe cases the microscopic reaction can readily be distinguished from any of the common types of encephalitis.

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## INDUSTRIAL MEDICINE'S CHALLENGE TO THE INTERNIST

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LOS ANGELES

Industrial medicine was conceived by the humane forces of an earlier day, which demanded care for the workman with mangled limb, crushed skull or broken back. It was born in the operating room, and its swaddling clothes were bandages and sutures. It was nurtured through the years by the surgeon, with the hygienist and the engineer contributing some of its clothing. Today, in its more mature appearance, it so strikingly resembles its guardian that the profession as a whole recognizes the characteristics of industrial surgery only. The diseases resulting from industrial hazards escaped the attention of the social forces, labor interests and law makers. Occupational disease, usually being insidous in character, lacked the pyrotechnics of trauma.

Inevitably, however, under gradual liberalization, certain states included occupational disease within the compensation code. Today approximately eighteen states admit all, or a specified list, of diseases as compensable if adjudged so. This admission of disease to the code, however, has had little or no effect on the industrial medical set-up, which remains surgical in type. The majority of plants and of railroads and other industries, as well as of insurance carriers, delegate to the surgeon the authority for diagnosis and treatment. Only in rare instances is this responsibility shared with a purely medical confrère. I do not wish to be misunderstood. I cannot sufficiently praise the industrial surgeon for his development of this branch of service to a high plane. He has no more right, however, to dispose of the occupational disease than has the internist to remove the gallbladder. Nor, in fairness to him, does he desire to do so. Inceptive circumstances forced him into the position he now occupies.

If, as will be illustrated later, the diagnosis of occupational disease requires trained diagnostic ability, why has the internist not been attracted to this field? The roster of industrial surgery is replete with the names of men famous in this field, who stand comparable to the surgeons of general medicine. But where are the Austin Flints, the Peppers, Cabots or Meakins of internal medicine? As indicated in the opening lines, circumstances commandeered the surgeon and he responded nobly, but failure earlier to recognize the extent and the importance of occupational diseases delayed the entrance of the internist. In addition, certain barriers repelled both.

Foremost of these were the stigmas attached to this form of practice. One was made to feel that he was admitting defeat when he entered this field. He was led to believe he had sold his medical birthright for a mess of the charlatan's pottage. Among the unenlightened this opinion still exists. Would that there could be gathered into some vast assemblage the entire profession to hear another Osler panegyrizing the pioneers in this field who shed hypocrisy and criticism, eventually to write one of the most brilliant chapters in modern medicine.

Another barrier has been the pattern of medical education. A few didactic dissertations, crowded grudgingly into a course on preventive medicine and hygiene, constitute the student's sole contact with any phase of industrial medicine. That such contact is negligible is evidenced by the latest report of the Council on Medical Education and Hospitals, in THE JOURNAL for April 23, which discloses the fact that, of the seventy-eight medical schools surveyed, only eighteen have a full time department of preventive medicine and hygiene. Only four schools have a course which emphasizes industrial hygiene, and only one that I know of has a course in occupational diseases. Nowhere in that report is the neglect to teach industrial medicine lamented.

It is apparent that the educational system has lacked vision when it is realized that 90 per cent of the students will have industrial contacts at some time in their careers. Postgraduate instruction is similarly missing. At the postgraduate symposium in Chicago last February, every angle of this subject was discussed, but no one championed a graduate course in occupational diseases. Praise was bestowed on the high standard of graduate instruction promulgated by state and county societies, but no one indicated that these groups constantly fail to allot time to occupational disease in their graduate courses. Even conventions held in the name of industrial medicine are not medical but chiefly surgical in character. I have collected twenty programs of meetings held in the name of industrial medicine within the past two years and, of the 198 papers read, only twenty-nine dealt with occupational disease.

The 1936 Fortnightly of the New York Academy of Medicine was a course offered for the study of "trauma, occupational disease and hazards." Of the more than twenty-five papers read, less than five dealt with diseases of occupation. Perusal of the program of the American College of Physicians, which met in April—truly a postgraduate session—fails to disclose a single

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correlation between the diseaser under discussion and those of occupation. At the California state medical meeting in May, the program of the section on industrial medicine disclosed the ridiculous brevity of six papers. Three were statistical; three were surgical. This is pathetic when occurring in a state where, from the beginning, occupational disease has had a broad coverage in the compensation code.

A third deterrent factor is the indifferent attitude displayed toward this field by the medical press. One suspects that articles on industrial medicine are rejected as so much trivia. If the practitioner is to be informed of existing problems in industrial medicine, it must be through our universally read periodical.

What is this exigency which occupational disease presents? What demand is created by it that the surgeon, hygienist or engineer cannot fulfil? It is diagnosis: diagnosis of innumerable conditions outside surgical experience and beyond the stage of preventive medicine. It is rendered absolutely paramount by the requisites of the compensation law. Basically the same in all states, a condition to be compensable must arise out of and in the course of employment. It must be distinguished from diseases which occur in spite of one's occupation, not because of it. On this distinction rests the whole structure of workmen's compensation. Time prohibits the verbal screening of this pantomime as enacted by occupational disease in the theater of industry. A terse paragraph picturing this parade of paradigms is necessary, however, to further the theme of this thesis.

With the exception of actual trauma, probably the most frequent condition to confront the industrial physician is pain in the lower part of the back. Usually it is not compensable and too frequently is incorrectly diagnosed. Differentiating a sprain of the back from myofascitis, referred pain from kidney or gallbladder, tuberculosis or a malignant condition of the spine, pain in the cord from syphilis or pernicious anemia, a tumor or abscess, or a congenital or structural derangement tests clinical acumen to the fullest. Silicosis may simulate tuberculosis, cardiac decompensation, bilateral bronchiectasis, asthma, a malignant process or mycotic infection. The heart presents prodigious problems in this field. The sudden death of a workman is frequently attributed to trauma, when in reality a fall, injury and subsequent death are often the result of aneurysm, ruptured valves, coronary occlusion or cerebral hemorrhage. Estimation of effort as a causative factor in cardiac accident is a frequent problem in industry, not commonly arising in general practice. The presence of diabetes, syphilis or perivascular disease must be determined in the case of nonhealing fractures, wounds or resistant ulcers. Time prevents discussion of anthrax, actinomycosis, undulant fever and tularemia as occupational conditions. The dermatoses are abundant and confusing. Lead, arsenic and mercury absorption mimic organic disease. The deleterious effects of noxious gases and solvents simulate organic disease.

This brief discussion is only one reel of the entire picture but is sufficient to indicate that the situation demands keen diagnostic perception. Does it seem reasonable that the surgeon, occupied with surgical diseases and trained in surgical technic, should be considered capable? Can the practitioner, neck high in the ills of his community, fill this position? Can the industrial physician, engaged in the practice of some industrial surgery and some community surgery and in a general practice, be relied on? Is it not obvious that the desideratum is the internist?

A further challenge to the internist from industrial medicine arises out of the present social unrest in America. Social security, old age pensions, unemployment insurance, health insurance and other forms of the vast socialization program will, of necessity, affect industrial medicine. I have stated that only eighteen states today have some form of compensation for occupational diseases. How long is this status likely to prevail? A socially minded government, an ever aggressive labor organization and a socially conscious workman will soon force into being throughout all the states compensation for all types of occupational diseases. When this occurs in the states as yet unacquainted with this problem, what part of the profession can be most quickly relied on to differentiate between communal ills and those arising from industrial hazards? Furthermore, compensation insurance is in grave danger of becoming too broad. Unless the profession has the proper perspective and understands the philosophy behind compensation, this form of practice will extend into social insurance and thence into state medicine. Thus the internist may be the buffer between organized medicine and the actuality of state medicine. On his ability to differentiate the natural ills of life from those arising from occupation may depend the preservation of general practice.

Anticipating the widespread acceptance of the occupational diseases within the compensation code, a few prophetic voices have intimated that when this occurs the burden should be delegated to the community physician. I most emphatically protest that idea. The functions of the general practitioner have been well defined by time and tradition. Seventy-five per cent of the population still depend on him for their care and need him just as he is. To impose on him the additional diagnostic problem entailed by the occupational ills of fifty million workers, not to mention the paper work involved, would overtax his time and capabilities. In addition, in protesting I am mindful of the welfare of the workman and the rights of the carrier. The reason for this objection can be illustrated by a few random cases.

Stooping to pick up a board, a workman experienced disabling pain in the back. Cursory examination by his physician resulted in a diagnosis of sprained back; physical therapy was prescribed and ten weeks' compensation awarded. A subsequent check-up revealed a malignant process of the spine.

An employee of a pottery company was sent to a nearby industrial surgeon because of a cough, loss of weight and increasing fatigue. The surgeon's technician made roentgenograms of the chest. The films appeared grossly abnormal. Knowing a silicosis hazard existed where this man was employed, the surgeon combined this fact with the abnormal films and the symptoms to conclude that the man had silicosis. Rest was ordered, and eight months' compensation resulted. Referred examination revealed the pertinent fact that the man was a shipper of the finished, boxed product and had been employed only one year and never before where there was a silicosis hazard. A sister with whom he lived had died two years previously of tuberculosis. Tests of his sputum were positive for tuberculosis, and the roentgenograms showed cavitation but no indication of silicosis.

On the other hand, a woman aged 36, who had been employed for fourteen years by a manufacturer of abrasive soap, consulted her community physician because of severe and increasing dyspnea. Cardiac decompensation was the diagnosis. Complete rest was ordered and digitalis administered. No compensation was awarded. Constant rest and gallons of digitalis resulted in no improvement and a consultation. The girl had advanced silicosis. When informed, her first physician was at a loss to connect soap making with silicosis.

A community physician diagnosed multiple sclerosis as lead poisoning because examination showed lead absorption, which, however, was normal; it did not show any lead intoxication. A baker went uncompensated for ten months for an asthmatic condition due to the wheat flour with which he was in daily contact. I cite these few cases not as indictments against the practitioner but as instances involving factors ordinarily outside his training or experience.

The American Medical Association has wisely insisted that neither the employer nor the insurance carrier shall discriminate against the community physician in favor of one of his own choosing. In full accord, my proposal does not violate that principle. There is no violation of that principle when the family physician refers a patient with an unrecognized heart ailment to the cardiologist for diagnosis. Once the diagnosis is made, the patient returns to his own physician for his after-care. The same policy is carried out with many other conditions requiring a diagnosis. The proposition that I advance is similar. In every city or community let there be formulated a list of the recognized internists or diagnosticians. Have this group certified as to fitness by the American Medical Association. They should be independent of contract or affiliation with any employer or carrier. Permit the employee or patient free choice of any one of this group. A recognized body having thus been established, let every patient with a questionable diagnosis or an estimated temporary disability of two weeks or longer be referred to one of this group for diagnosis. Once that is done, the patient is to return to his community physician for treatment as indicated. If the internist is denied the right to treat the patient, then the existing tendency to make the condition compensable in order to obtain fees for weeks of treatment will be removed. Equity to the workman and the carrier will be assured.

In conclusion, I offer no apology that this paper has not dealt with guinea pigs or test tubes. Medicine needs guidance as well as science. Industrial medicine needs not only guidance but more abundant recognition as one of the important medical specialties. This recognition will not come through the beating of tom-toms by its exponents. It will not come through articles read within this section or appearing only in journals of industrial medicine. It must be obtained by focusing the attention of the entire profession. Nor is the mere expression of thought sufficient. It is time for action by the parent body, the American Medical Association.

The manner of action and the answer to the challenge outlined in this thesis had, I believe, its inception one year ago, when too tardily the Council on Industrial Health was admitted to the American Medical Association. At its first meeting in December it was decided to "proceed slowly." Such a decision is inconsistent with the urgency of the situation. This council should immediately join with the Council on Medical Education and Hospitals to bring about a readjustment of the medical school curriculum in order that occupational disease may be elevated to proportional importance. It should insist on a fair representation in the postgraduate programs of the county societies as well as in the sectional programs of the state and national meetings. Cooperation with the American insurance group should be sought so that common problems can be solved. Through such mediums—the medical school, the postgraduate system, the medical press and the insurance group—this new body may so function as to induce the present internist, or the future physician, to accept the challenge industrial medicine offers. I confidently anticipate the advent of the occupational disease consultant.

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## ABSTRACT OF DISCUSSION

DR. LEOPOLD BRAHDY, New York: We are indebted to Dr. Johnstone for this statement of a deficiency in industrial medicine of which we have all been aware, but no one has previously formulated it or outlined a program to remedy it. The major part of industrial work still is and will continue to be surgical in nature. The medical departments of a few large employers have for many years had consulting internists especially interested in occupational diseases; in other words, the occupational disease consultant has arrived, although until now he has had no specific name and still lacks recognition. What Dr. Johnstone advocates is coming to pass, though much too slowly. In Mexico I found that occupational diseases have long been accepted as a definite medical specialty, and the medical school of Mexico University devotes more time to this subject than any of our schools. In 1935, at the International Congress on Occupational Disease and Injuries in Belgium, two things that bear on this question impressed me: first, the small proportion of Americans (I think the total number was six); secondly, that our colleagues of other lands who specialized in occupational diseases held important positions in their profession, their medical schools and their governments, much more than those in this specialty in the United States. This confirms Dr. Johnstone's thesis of the need of better recognition in the United States. The presence of consultants in occupational diseases of the medical staff of a few large employers is not sufficient. About half of all production is by small employers, those who have 200 employees or less. Such employers necessarily seek medical advice from the community physician, the same physician who takes care of their workers' injuries. These practitioners, even if they attended one of the few medical schools that have courses in industrial hygiene, cannot be experts on cases they so seldom see. These physicians should consult specialists in occupational disease problems, just as they consult brain surgeons or ophthalmologists. When an occupational disease consultant is to be found in every industrial community and adequately recognized, these smaller plants which employ the majority of our workers will be able to obtain the benefit of expert advice. Specialization in occupational disease by the internist is essential because the field is large and expanding. Diagnostic ability is the keystone of the specialty. The physician must not only diagnose any known occupational disease; he must be able to recognize promptly a new clinical entity, one just born as a by-product of the dizzy multiplication of industrial products and methods. To do that necessitates a degree of clinical acumen which cannot be required of the busy practitioner. A course in occupational diseases should be part of every medical curriculum.

DR. DWIGHT O'HARA, Boston: I wish to say a word in defense of the medical school curriculum. This call for more time is not unique; it has come within recent years from a dozen groups who have settled down to the job of expanding their own interests. I do not imply that such expansion is not salutary, but the recommendation that medical school courses be expanded to include more didactic instruction in these special

lines is against the present trend in medical education. The call is now for less rather than more didactic instruction. We do not believe that we can make any kind of specialists by haranguing our classes for sixteen, thirty-two or sixty-four hours in special subjects. We already cover much of industrial medicine in other courses. A Colles fracture is the same whether it is sustained in the kitchen or in the factory and lead poisoning is the same, wherever the lead arises. Other courses emphasize channels of entry and the influence of age and sex for most industrial poisons. I favor the development of industrial medicine but in the same way that I do the development of preventive medicine; that is, as a point of view in a much larger conception of environmental influence. Also there is a point of diminishing returns in the development of any specialty. When any specialist who does not deal directly with the chest becomes so specialized that he allows himself to make the statement that he "knows nothing about chests," he ceases to be as effective a doctor as he was before he forgot what little he may have learned about chests in the medical school.

DR. AUGUST F. KNOEFEL, Terre Haute, Ind.: Having been born and raised with the industrial commission in our state, I enjoyed the remarks that have been made. The previous discusser said that there is no difference between the Colles fracture of the man at the plant and the one of the wife at home. There is a big difference, and that is the psychoneuroses that attended the fracture at the plant. It makes a big difference when the time for adjudication comes up. There is a place for this organization. My reaction is that if it is to do the greatest good it should become more scientific and less sociologic. There are doctors who still believe that if a person chews a lead pencil he will have lead poisoning. That may be an exaggeration. A person walks through a public garage and the next day has a headache, nausea and vomiting—carbon monoxide poisoning. All a man has to do to testify before an industrial commission is to be a graduate of medicine and registered in his state. We can bring in the thyroid expert or some one who knows things from A to Z, but his testimony is of no more value legally than the testimony of the individual who lives out in Podunk.

DR. A. T. MCCORMACK, Louisville, Ky.: We are hearing about the necessity of devoting more time in the undergraduate courses to training for the specialties. I attended the other day a conference on maternal health in Washington and was impressed with the fact that the speakers, several of whom had each had thirty years' experience as teachers of obstetrics in great state universities, testified that there was practically no one in their states qualified to deliver a woman, that only those who had passed an examination by the American Academy of Obstetrics were so qualified, and formal resolutions were passed that nobody could be called in consultation in obstetric cases unless he had that qualification. I am sympathetic with the idea that the man who holds himself out as a specialist should know his subject. The fact, however, has been brought out that 75 per cent of all the ills that mankind has had have been treated by the general practitioner; and yet among the medical schools of the United States there is only one, so far as I know, that has a general practitioner in the faculty, and that is the Albany Medical College. I believe that if we teach the student while in school in his premedical, cultural education, while he is in the technical school, enough facts on which he can base the ability to observe and to reason from his observations, we have done as much for him as we can. Let's put the emphasis on graduate work for the men peculiarly adapted to the specialties which we want our disciples to be taught and to learn. There can be no question that the internist is important, that he has a distinct and definite place in the vast field of industrial medicine. But only that internist will really succeed who, in addition to his scientific knowledge, has the ability to differentiate the different psychoses, the different neuroses, the selfishness and sordidness of the people who come before him, and to exclude those things that need to be excluded and to keep before him this whole complex situation which has been brought about by our compensation laws and other things. Let's not get the idea that we are going to be able to develop, full fledged from our undergraduate medical schools, specialists who will make any serious contribution to human welfare.

# CHILLING OF THE BODY SURFACES

## ITS RELATIONSHIP TO AURAL AND SINUS INFECTIONS

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It is doubtful whether any subject in medicine in the last decade has stirred more interest and caused more study than the etiology of infections of the upper part of the respiratory tract. Through recent improved understanding of the autonomic nervous system, the biochemical processes and the bacterial flora constantly present in the nasal cavity and its adnexa, much of the fog of empiricism has been dispelled. A cardinal factor not to be ignored, however, is that the human organism must maintain a constant average temperature of 98.6 F. (37 C.), for any considerable degree of deviation from this average for appreciable periods of time will result in morbid changes.

Cold water has a veritable appetite for heat. Since the ratio of conductivity of water to air is 27 to 1, it follows that water takes heat from the body twenty-seven times faster than does air. The lack of a compensating mechanism for the maintenance of an average normal temperature in any medium colder than his normal surroundings is conspicuous in man. Many arctic birds maintain a normal temperature above 102 F. (38.9 C.) throughout continued periods of exposure to icy waters, as do also the arctic Mammalia, yet man's loss of body heat during submersion for only fifteen or twenty minutes in water at a temperature of 70 F. (21.1 C.) may be five times the normal basal rate. Mudd, Goldman and Grant [1] reported the striking effect of this loss of body heat on the nasal mucous membranes. In their experiments, carried out by placing in the nares a sensitive instrument devised for registering temperature, they recorded depressions as great as 10.8 degrees F. (6 degrees C.), their observations indicating the great amount of vasoconstrictor response in this area.

This tendency to rapid loss of heat owing to physical conditions that promote such loss forms the basis for this study. Its practical application relates to the ordinary causes of the common cold, in particular bodily immersion such as swimming and bathing, and also exposure to excessive cooling by drafts, from damp clothing and the like.

One of us [2] observed the effect of chilling on 250 children under 13 years of age by taking their temperatures before and after a period of forty-five minutes' duration devoted to swimming in an indoor pool with the temperature of the water at 73 F. (22.8 C.). In only thirty of this number was a normal temperature maintained; in many there occurred a drop to as low as 95 F. (35 C.).

It has been brought out previously that well tended swimming pools do not constitute the bacterial menace often attributed to them. Bacteria are of course normally and constantly present in the upper respiratory

Read before the Section on Laryngology, Otology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Mudd, S.; Goldman, A., and Grant, S. B.: Reactions of the Nasal Cavity and Postnasal Space to Chilling of the Body Surface, J. Exper. Med. 34:11 (July) 1921.
2. Taylor, H. M.: Sinusitis and Swimming, J. A. M. A. 85:7 (July 4) 1925.

passages, but they may multiply to pathologic proportion in the person whose resistance is lowered.

Kuntz [3] made clear the interrelation of the innervation of the peripheral blood vessels and the mucous membranes. This autonomic control of vasoconstriction and vasodilatation forms the basis of the physiologic balance between the splanchnic and the peripheral areas. Thus, when stimulation by cooling results in peripheral ischemia, the mucous membranes undergo a similar experience; prolongation of this condition serves to throw out of balance the nicety of integration existing under normal metabolic phases and accounts for the ability of ordinarily avirulent organisms to overcome the obstacles of tissue immunity at the portals of entry.

## EXPERIMENTAL STUDIES

In the present study the most important single factor regarding the establishment of infection is that during exposure peripheral vasoconstriction is prevented by the three animals a second exposure to cold caused an even more decided leukopenia than at first.

Moon, Lieber and Kennedy [5] noted that, when histamine-like substances are present in the blood, a leukocytosis occurs. This observation would seem to indicate that in the cases observed by us, in which leukopenia developed in both animals and human beings after chilling in the absence of muscular activity, there was no histamine allergy to cold such as that recently reported by Horton and Roth.[6]

In connection with his work as a member of the Committee on the Otorhinologic Hygiene of Swimming of this section of the American Medical Association, one of us [7] reported in 1936 the observations on a group of swimmers that are set forth in table 2. Eight lifeguards at Jacksonville Beach, Fla., were subjected to swimming for forty-five minutes in ocean water at a temperature of 68.5 F. (20.3 C.). The weight, temperature, blood pressure and blood count of each swim-

TABLE 1.—*Changes in the Hemogram of Guinea Pigs After Chilling*

| | Animal 1 | | | Animal 2 | | | Animal 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | After* | | | After | | | After | |
| | Before | 1st Test | 2d Test | Before | 1st Test | 2d Test | Before | 1st Test | 2d Test |
| White blood cells | 8,250 | 6,850 | 6,750 | 9,850 | 7,400 | 7,250 | 8,000 | 6,300 | 4,400 |
| Polymorphonuclears | 70 | 60 | 67 | 82 | 77 | 49 | 62 | 39 | 44 |
| Lymphocytes | 19 | 60 | 32 | 18 | 23 | 51 | 30 | 57 | 53 |
| Monocytes | 3 | .. | .. | .. | .. | .. | 1 | 1 | .. |
| Eosinophils | .. | .. | 1 | .. | .. | .. | 5 | 3 | 3 |
| Basophils | .. | .. | .. | .. | .. | .. | 1 | .. | .. |

* Time elapsing between exposure tests about one-half hour.

TABLE 2.—*Effect on Blood Cell Count in Marathon Life Savers' Race, Jacksonville Beach, Fla., Sept. 9, 1935*

| | Before | | | | | | | | | After | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Name | Red Blood Cells | White Blood Cells | Juveniles | Stab Cells | Segmented Cells | Lymphocytes | Monocytes | Basophils | Eosinophils | Red Blood Cells | White Blood Cells | Juveniles | Stab Cells | Segmented Cells | Lymphocytes | Monocytes | Basophils | Eosinophils |
| Deloach | 4,530,000 | 7,450 | 0 | 13 | 44 | 31 | 0 | 0 | 0 | 5,130,000 | 18,200 | 3 | 15 | 73 | 5 | 1 | 0 | 0 |
| Perkins | 4,320,000 | 5,700 | 4 | 15 | 34 | 41 | 1 | 0 | 0 | 5,340,000 | 19,900 | 2 | 23 | 68 | 7 | 0 | 0 | 0 |
| Horton | 4,448,000 | 6,700 | 2 | 26 | 32 | 39 | 0 | 0 | 0 | 5,830,000 | 21,750 | 5 | 28 | 67 | 2 | 0 | 0 | 0 |
| Penn | 4,560,000 | 11,000 | 0 | 26 | 48 | 26 | 0 | 0 | 0 | 5,300,000 | 23,750 | 2 | 30 | 53 | 15 | 0 | 0 | 0 |
| Miller | 4,610,000 | 8,500 | 0 | 20 | 30 | 50 | 0 | 0 | 0 | 5,470,000 | 17,200 | 6 | 18 | 44 | 32 | 0 | 0 | 0 |
| Crenshaw | 4,210,000 | 5,650 | 0 | 21 | 41 | 38 | 0 | 0 | 0 | 4,650,000 | 20,400 | 7 | 25 | 51 | 16 | 0 | 0 | 1 |
| Clark | 4,660,000 | 6,700 | 2 | 29 | 45 | 23 | 0 | 0 | 0 | 5,350,000 | 18,800 | 2 | 30 | 34 | 32 | 0 | 0 | 2 |
| Liddell | 4,490,000 | 8,000 | 0 | 6 | 58 | 35 | 1 | 0 | 0 | 5,580,000 | 12,250 | 2 | 12 | 66 | 20 | 0 | 0 | 0 |

muscular activity, and it follows that infection is therefore less likely to occur. In an experiment with animals, three healthy, mature guinea pigs, weighing approximately 250 Gm. each, were placed for half-hour periods in an ice refrigerator in which the temperature was 59 F. (15 C.). As soon as they were removed, blood counts were made with specimens of freely flowing blood from the veins of the ear. The observations made and previously recorded are set forth in table 1 to show the rather striking changes occurring in the hemogram.

The conclusions to be drawn from this experiment are that chilling without exercise produces a leukopenia of the polymorphonuclear neutrophilic type. As stated by Trommsdorf,[4] the phagocytic powers of the blood cells are definitely diminished. This observation was further substantiated by the death of one of our animals within twenty-four hours, and at autopsy the presence of bronchopneumonia was noted. In each of mer were ascertained prior to and immediately after the period of swimming. All the participants after the swim exhibited a diffuse generalized purplish hue. Their nail beds were moderately cyanotic, as were their lips. There was an average reduction of 4 degrees F. in the rectal temperature. The increase in the erythrocyte count ranged from 700,000 to 1,500,000 red cells. The leukocyte count was consistently increased by from 3,650 to 24,750 white cells. The Schilling index was virtually normal. There was no loss of weight. Both the systolic and the diastolic blood pressures were increased, but the greater average rise was in the diastolic pressure, being from 20 to 30 points. There was no such consistent increase in the systolic pressure.

In a third experiment, made at Jacksonville, Fla., in September 1937, three bathers remained submerged in a pool for fifty minutes, keeping reasonably quiet

3. Kuntz, Albert: The Autonomic Nervous System in Relation to Otolaryngology, J. A. M. A. **107**: 334 (Aug. 1) 1936.
4. Trommsdorf: Arch. f. Hyg. **59**: 1, 1906.
5. Moon, V. H.; Lieber, M. M., and Kennedy, P. J.: Histamine and Leukocytosis, Arch. Path. **20**: 175 (Aug.) 1935.
6. Horton, B. T., and Roth, Grace M.: Collapse After Swimming, Proc. Staff Meet., Mayo Clin. **12**: 7 (Jan. 6) 1937.
7. Taylor, H. M.: Report of Committee on Otorhinologic Hygiene of Swimming, Tr. Sect. Laryng., Otol. & Rhin., A. M. A., 1936, p. 300.

by refraining from exercise. The temperature of the water was 72 F. (22.2 C.). The observations set forth in table 3 indicate the distinctly depressive effect of chilling the body surfaces without concomitant exercise. The polymorphonuclear leukocytosis, so evident in the second experiment, was totally lacking here; indeed there was even a relative leukopenia, both as to the total number of white cells and as to the polymorphonuclear neutrophil count. It was also observed that the temperature of the body tended to drop and the pulse rate to slow.

## CONCLUSION

It is evident from these experiments that chilling of the body surfaces without compensation leads to morbid changes within the body. They are caused (1) by peripheral vasoconstriction with attendant peripheral stasis and anoxemia, (2) by lowered leukocyte response, both total and polymorphonuclear, and (3) by impairment of the phagocytic capabilities of the fixed tissue cells, including that of the nasal mucous membrane.

TABLE 3.—*Effects of Chilling Without Concomitant Exercise*

| Name | Temperature* | | Pulse Rate | | Blood Pressure | | Total Leukocyte Count | |
|---|---|---|---|---|---|---|---|---|
| | Before | After | Before | After | Before | After | Before | After |
| Pittman | 98.3 | 95.4 | 80 | 68 | 126/80 | 128/80 | 8,300 | 8,400 |
| Portson | 98.3 | 97.0 | 70 | 72 | 118/90 | 120/88 | 9,250 | 8,150 |
| Horton | 98.5 | 97.0 | 70 | 60 | 120/80 | 130/80 | 7,100 | 6,300 |

* Temperatures were taken by rectum.

One of the immediate results of these changes is the predisposition to infections of the upper part of the respiratory tract, the paranasal sinuses, the eustachian tubes and the middle ear.

111 West Adams Street.

## ABSTRACT OF DISCUSSION

DR. EDWARD CECIL SEWALL, San Francisco: The authors have shown the physical changes caused by the chilling of the body. He has suggested that the blanching of the respiratory surfaces makes one liable to respiratory disease. I am in general agreement but believe that the discussion may be amplified and qualified. One must distinguish between normal persons and those who harbor chronic sinus infection. I believe that, ordinarily, chilling only induces respiratory disease in those who already harbor respiratory infection, most often in the sinuses. The normal person is but little adversely influenced by a reasonable degree of chilling. Such a person is exemplified by John Muir, who, soaked to the skin, slept on Alaska glaciers repeatedly. He arose in the morning, wrung out his clothes and went his way. He rarely took cold. He was a normal, healthy person. He harbored no chronic sinus infection. He could not have exposed himself in such a way if he had. He carried an immunity granted by his last true "cold" from which he had fully and completely recovered. He was vulnerable to upper respiratory infection only when that immunity had run its course, ordinarily varying from six months to several years. With lapse of his acquired immunity, chilling might have favored susceptibility to respiratory infection. Even that, however, is open to question, as common experience shows that true colds travel with little reference to chilling and exposure. I constantly find and study people of this type who are free from all sinus infection. Usually sturdy folk, they are little influenced or inconvenienced by chilling. The great majority of people, however, harbor chronic sinus infection. It is in this type that the work of the authors is of great importance. Such individuals have been shown by Kistner and others to harbor bacteria constantly in the deeper layers of their sinus mucosa. These germs are held in leash by the forces of immunity generated in the body and carried in the blood. They always act as irritants. Under warm climatic and other favorable influences the bacteria show little activity, measured by the amount and character of the discharge they always produce. Chilling of the body, as Drs. Taylor and Dyrenforth have shown, causes certain physical changes that relax the vigilance of the body guards toward these incorrigibles. The latent bacteria show immediate activity. Some of you already may have recognized the effect of our local summer "refrigerating system" of fog and brisk sea breeze.

DR. JOHN J. SHEA, Memphis, Tenn.: To comprehend this paper it is necessary to study it in detail after reading the papers that have been written relative to the hygiene of swimming. There exists in the human body a mechanism that controls heat production and elimination, a second system that is a barrier controlling the migration of blood cells from the hematopoietic system into the general circulation, and third a biochemical balance that maintains our normal $p_H$ irrespective of whether we take foods that are acid or foods that are alkaline. Whenever one of these is disturbed all three of them will be disturbed and in the chilling action the heat mechanism is influenced, which in turn disturbs this barrier, of the physiologic action of which little is known. There is always stored up in our hematopoietic system sufficient matured and immatured blood cells so that if they accidentally migrate into the peripheral circulation there will be a blood dyscrasia. The answer to why we are susceptible to colds after chilling may be this interrelationship between the hematopoietic system and the buffer, which maintains our biochemical balance. The application of the paper is this: If any one of us would wrap ourselves in a wet blanket and go into the basement of our home for forty-five minutes or an hour we would certainly end up with a cold or possibly pneumonia, provided we harbored the proper bacteria. A child subject to recurrent infections of the sinuses, middle ears and mastoid should avoid the promiscuous habit practiced at these pools of children playing in wet bathing suits, which lowers their resistance and brings about a recurrence of sinusitis or middle ear infection. The child who goes to California or Florida in the winter to convalesce from these infections should not be allowed to swim or even wade but should limit his activity to the beach.

DR. BURT R. SHURLY, Detroit: Since the days of the vulnerable heel of Achilles, we have known that many individuals have a peculiar idiosyncrasy to a chilling of the body. This chilling is commonly caused by a draft on the feet, when low shoes are worn, or when the feet have inadequate protection. There is the chilling after a haircut and shampoo, the chilling from insufficient clothing, the susceptibility to chilling after the sun goes down, with the attendant development of the common cold or congestion of the turbinates, with various hyperemic manifestations of change. We know that sensitiveness to cold is not as common as sensitiveness to heat. The former can be relieved by the application of heat or by exercise. Persons with heat sensitiveness react during the warming up process but are made worse by heat. In 1909 Wallace reported a case in which, after the ingestion of ice cream and a glass of cold water, a severe attack of asthma, watery discharge from the nose and eyes, cyanosis, urticaria and collapse occurred. Probably diathermy or some other form of heat, mental exercise or excitement would have relieved the paroxysm. Asthma caused by cold, as well as urticaria, is related in many case reports. It is not uncommon to find a nasal mucous membrane sensitive to local heat relieved in a refrigerated room, by a cold compress or by the inhalation of cold air. In some persons thermic sensitiveness is closely related to infection, rising with slight changes in the weather. The true infection may be simulated by these sharp reactions. This is not always lowered resistance but a lack of vasomotor tone in the thermoregulators of the body. Some of it is endocrine in its lack of response; some of it is in those who carry a chronic infection of the sinuses or manifest allergic phenomena. These persons become forewarned by experience; they have chilling after prolonged bathing or swimming, with a cyanosis and skin reactions, a lowered temperature, from 92 to 95 F., which denote a failure in vasomotor response to chilling of the body. The old treatment—a mustard foot bath with 10 grains of quinine and 10 grains of Dover's powder—was an ancient therapeutic measure to counteract the common cold. The reinforcement of circulatory deficiencies has for years

been recognized by the use of the hot lemonade or a hot toddy at bedtime following chilling of the body. The first stage of pneumonia—a congestion of the lung—should be met with prompt therapeutic action or even a hypodermic sedative to restore the vasomotor action.

DR. H. MARSHALL TAYLOR, Jacksonville, Fla.: Dr. Sewall comments on the fact that Mr. Muir was peculiarly free from sinus infection during his arctic adventures. As long as one can maintain his normal temperature in such an environment, his resistance is not necessarily lowered.

## EDUCATION A MAJOR NEED IN ADEQUATE MEDICAL CARE

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Adequate care for the sick presupposes the existence and the use of adequate facilities. Both economics and education are integral parts of the problem of adequate medical care. If the economic structure of society were such that all could afford adequate service, many would not get it through lack of proper information. The individual must be able to recognize the need of seeking service, he must avail himself of the resources available, and either he or some one for him must finance the service. Care by physicians, dentists, hospitals and nurses and the providing of pharmaceutic products are the chief needs, and the bulk of all moneys expended are for these services.

Disease is of two types, the acute and the chronic. The demands made by chronic illness are greater because of the long periods of disability and often because of the patient's failure ever to resume his customary work. If the patient is the supporter of a family, the situation is even worse.

In the older communities, in which, because of the age distribution, many of the citizens are incapacitated with chronic disease, the problem is becoming a real burden on the community. If the community is to attempt a control of chronic disease, it must avail itself of all information at its disposal regarding the problem. Data from the Massachusetts survey of chronic diseases and the Massachusetts cancer program are presented in this paper in the hope of partially clearing up some of the confusion on the subject.

The eradication of chronic diseases is extremely improbable, but to secure delay in the onset of some of these diseases and to prevent others seems a reasonable objective. Studies have shown that the onset of many of these diseases occurs to too great an extent in early middle life. In the Massachusetts study of chronic diseases approximately 20 per cent of persons between the ages of 40 and 50 were found to be affected If the age of onset could be extended to beyond 60, the twenty year increase in the span of health would mean increased working efficiency, lower bills for sickness, less drain on the family income and improved general well being of the individual.

In considering the needs of the American people for medical attention, the mere chronicling of the diseases present, such as has been done in the majority of surveys, gives a reasonably reliable measure of morbidity and the percentage of the population which does not receive medical treatment. Of those who do not receive medical care, however, there are some who do not need it, such as the blind man and the one-legged man. In planning any program for improving the condition of persons not receiving medical care, this factor needs consideration.

Another factor of importance is the adequacy of the service of persons who are receiving medical attention. Do they receive as much care from the physician as is necessary? How well is the physician able to meet their demands? Other phases of the problem require a discussion of hospitalization, nursing care, dental care, cost of pharmaceutic products and the cults.

The scope of this paper is limited to the presence or absence of medical care during a one year period among persons with chronic disease. The number of physicians' calls is not considered, nor is the adequacy of the therapy administered.

In the survey of chronic diseases conducted by the Massachusetts Department of Public Health in 1930, records were obtained from 15,000 persons over the age of 40. Of this number 4,337 (28.9 per cent) admitted having one or more chronic diseases. Of the sick, 63.7 per cent were under the care of physicians, 2.3 per cent were cared for by the various cults and 33.9 per cent had either self-administered treatment or no treatment. Subdivided according to economic status, those with a comfortable income employed physicians in 80.5 per cent of the cases, those with a high moderate income in 69.7 per cent, those with a low moderate income in 63.2 per cent and the poor in 58.6 per cent.

TABLE 1.—*Reasons for Lack of Medical Care Among Persons Who Had Received No Care for One Year*

| Reason | Comfortable | High Moderate | Low Moderate | Poor | Total |
|---|---|---|---|---|---|
| Felt condition not serious | 6 | 46 | 139 | 33 | 224 |
| Felt physician could not help | 3 | 54 | 289 | 92 | 438 |
| Fear | 0 | 1 | 4 | 2 | 7 |
| No faith in physicians | 0 | 4 | 30 | 21 | 55 |
| Economic reasons | 0 | 9 | 41 | 30 | 79 |
| Other reasons | 1 | 2 | 15 | 4 | 25 |
| Unknown | 0 | 8 | 8 | 4 | 20 |
| Total | 10 | 115 | 551 | 302 | 878 |

All the diseases and disabilities were not necessarily of equal importance in respect to the need for medical care. An attempt was made to separate the persons having conditions which it was felt required a physician's care from those for whom a physician could do little or nothing. This separation was necessarily arbitrary, but for practical purposes the group remaining after the persons with conditions which were not normal but for which there was probably little or no need of medical care were withdrawn is a far better criterion of the need for medical service. This group comprised 3,266 persons (21.8 per cent of the surveyed population). When subdivided by an economic basis, 20.1 per cent of those with a comfortable income were sick and 82 per cent of the sick had employed physicians during the preceding year, 19.8 per cent of those with a high moderate income were sick and 74.6 per cent of the sick had employed physicians, 20.9 per cent of those with a low moderate income were sick and 70.8 per cent of the sick had employed physicians, while 28 per cent of the poor were sick and 65.4 per cent of the sick had employed physicians. If treatment at the time of the survey had been used rather than medical care during the past year, the rates would be much lower but also less descriptive. The persons who had had no care during the preceding year were questioned as to their reasons (table 1).

If the figures for the reasons "felt condition not serious," "felt physician could not help," "fear" and "no faith in physicians" measure the need for education, approximately 80 per cent of the persons who did not employ a physician during the past year required education. If the reasons for delay are applied to the sick who needed physicians (3,266), the rates indicate that economic factors are not as important as education.

TABLE 2.—*Reasons for Not Having Physicians, Percentages*

| Reason | Comfortable | High Moderate | Low Moderate | Poor | Total |
|---|---|---|---|---|---|
| Need of education | 13.5 | 19.4 | 23.7 | 22.1 | 22.4 |
| Economic reasons | 0.0 | 0.0 | 2.1 | 9.0 | 3.0 |
| Others and unknown | 1.5 | 1.8 | 1.2 | 1.3 | 1.4 |
| Had irregular practitioners | 3.0 | 4.2 | 2.0 | 2.2 | 2.4 |
| Had physician | 82.0 | 74.6 | 70.9 | 65.4 | 70.7 |
| Total | 100.0 | 100.0 | 100.0 | 100.0 | 99.9 |

TABLE 3.—*Reasons for Delay*

| Reason | Percentage of Those Who Delayed | Percentage of Total |
|---|---|---|
| Negligence | 76.2 | 42.1 |
| Fear | 5.8 | 3.2 |
| Economic reasons | 4.5 | 2.5 |
| Miscellaneous | 13.5 | 7.5 |
| Less than two months' delay | .... | 44.7 |
| Total | 100.0 | 100.0 |

The need for a better informed public at all economic levels is indicated. Among the poor, approximately 10 per cent were deterred from having medical advice during the preceding year by financial reasons. Again it must be emphasized that having medical care does not measure adequate medical care. The interesting observation is that among the poor who had not employed physicians, those who gave reasons which indicated a need for education were twice as many as those who furnished economic reasons.

As confirmatory evidence, the ten year experience in the Massachusetts cancer clinics is cited. Massachusetts has conducted free diagnostic clinics for cancer for over ten years; free hospitalization has been furnished for the indigent and low cost hospitalization ($10.50 a week) for those able to pay. Free pathologic service has been given, and an educational campaign, based on the thesis that the local physician shall be the instructor to his community, has been in operation since 1934. There is no reason why any person should not receive an adequate diagnosis of cancer and adequate therapy provided he knows the need for seeking service and is willing to avail himself of the facilities.

The experience in Massachusetts demonstrates most conclusively that the keynote of cancer control is education. Records have been obtained from 4,159 persons who came to the diagnostic clinics and have since died of cancer. The living patients were not tabulated, but it is believed, on the basis of other studies, that if they had been included the results would not be far different. Of the 4,159 patients, 44.7 per cent delayed less than two months in consulting a physician after noting the first symptoms. Two months may be considered too long an interval to classify as no delay, but it has been arbitrarily chosen. Negligence was given as the reason for delay by 42.1 per cent of the patients, fear was given by 3.2 per cent, economic reasons by 2.5 per cent and miscellaneous reasons by 7.5 per cent. The only explanation for the percentage who furnished economic reasons would appear to be prudishness about using the state clinics, inability to find transportation to the clinics or lack of knowledge of their existence. The last-named reason bespeaks a need of more education.

After going to the clinic and receiving a diagnosis, some patients delayed further, although 85 per cent received treatment within one month.

Of the 227 persons who never reported for treatment, over one fourth were unwilling to admit the diagnosis of cancer. An additional 4 per cent claimed negligence, while 8 per cent complained of fear. If these rates are combined in the estimate of the need for further education, even for those who attended the clinics, 37.4 per cent of those who never accepted treatment were impelled by this reason, contrasted with 1.5 per cent who furnished economic reasons. These methods of appraisal indicate that a large part of the need for medical care is due to lack of demand, primarily because of failure to recognize and utilize the available service.

As a measure of what can be accomplished by intensive education, the experience of the Massachusetts cancer clinics is again cited. The intensive program began late in 1934, and a comparison of the years from 1934 to 1937 in the state as a whole and in organized communities is made. In towns where the cooperative cancer control committees are functioning well, there has been an increase of 44.6 per cent in patients with cancer referred by physicians, while in the state as a whole, including both organized and unorganized communities, the increase is 22.4 per cent. The percentage of persons who went to their physicians within the first two months of illness increased between 1934 and 1937 in the organized communities by 31.8 per cent, while in the state as a whole it increased by 27.3 per cent. The number of persons who came to the cancer clinics during the first five months of their disease increased 15.9 per cent in the organized communities and 3.2 per cent in the state as a whole. The number of physicians who use the pathologic service has tripled in the organized communities, while in unorganized communities it has only slightly more than doubled. This observation is especially significant because in some of the organized communities new pathologic services have been started.

TABLE 4.—*Period of Delay Between Diagnosis and Treatment*
(Massachusetts State-Aided Cancer Clinics)

| Reported for treatment within: | Percentage |
|---|---|
| 1 week | 57.5 |
| 2-4 weeks | 27.5 |
| 2 months | 4.8 |
| 3 months | 1.8 |
| 4 months and over | 2.9 |
| Did not report | 5.5 |
| Total | 100.0 |

TABLE 5.—*Reasons for Persons Dying of Cancer Without Reporting for Treatment*
(Massachusetts State-Aided Cancer Clinics)

| Reason | Percentage | |
|---|---|---|
| Unwillingness to admit diagnosis | 25.4 | |
| Negligence | 4.0 | 37.4 |
| Fear | 8.0 | |
| Economic reasons | 1.5 | |
| Physical condition | 36.8 | |
| Family problems | 2.5 | |
| Miscellaneous | 15.8 | |
| Total | 100.0 | |

It would seem that the method used in Massachusetts in combating cancer might well be extended to include other chronic diseases. The physicians of the com-

munities attempt to educate the people, and the state, in turn, furnishes supplementary service for the patients of the physicians.

SUMMARY

1. Of 3,266 persons with chronic disease whose records indicated the need for medical attention, 878 did not have a physician during one year preceding the survey.

2. For every one who gave his economic status as a reason for not employing a physician, 7.47 gave reasons which pointed toward a need for more information. Among the poor, this ratio was reduced to 1 giving economic reasons to 2.46 needing education.

3. Over half the persons who attended the Massachusetts cancer clinics delayed over two months, and the majority of them gave reasons which pointed toward a need for more education. The Massachusetts program cares for the economic needs, but the problem of delay is still acute.

4. The experience of the Massachusetts cancer clinics with persons who delayed obtaining treatment after diagnosis showed a similar need.

5. As a result of an intensive educational campaign on cancer conducted in Massachusetts for the past three and one-half years, part of the need for medical service has been reduced. A further reduction seems extremely probable.

CONCLUSIONS

The type of program conducted in combating cancer might be extended to other diseases. Whether the Massachusetts cancer program will be successful in other states remains to be seen (several are now trying it). Whether an extension to other diseases elsewhere is practical is problematic.

## Clinical Notes, Suggestions and New Instruments

### SEVERE HYPERCHROMIC MACROCYTIC ANEMIA OF PREGNANCY

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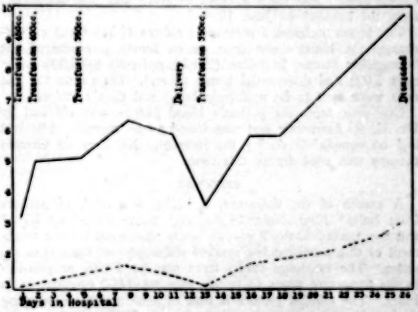
Mrs. A. R., an Italian housewife, aged 34, admitted to the hospital May 22, 1936, was a sextipara and septigravida, with parturition due May 30. For the previous two months she had noticed increasing weakness. Two weeks before admission she had begun to experience almost constant nausea, with frequent vomiting, and since then she had remained in bed. The weakness had increased to the point of dyspnea and palpitation on moving in bed. The skin had become yellowish and the urine scanty and dark. The bowels moved infrequently; the stools were brown, and there had been no diarrhea. For the previous week she had noticed numbness and tingling over the anterior surface of the right thigh, and on the day before admission she had a sudden attack of numbness involving the right side of the face and the right arm.

The diet had been low in protein and vitamins for economic reasons.

The patient's first child died shortly after birth. Since then she had had five normal pregnancies and no miscarriages. She had an appendectomy and oophorectomy in 1926. In 1930 she had suffered from rheumatism but had had no symptoms since. There was no history of syphilis, rat bite or exposure to industrial poisons. She had not received medication recently by mouth or by injection. The family history was entirely irrelevant.

At examination the temperature was 98 F., the pulse rate 96, the respiratory rate 20 and the blood pressure 135 systolic, 65 diastolic. The patient, who was obese, was sitting propped up in bed and was dyspneic on slight exertion. The skin was dry, with a lemon yellow tinge. There were no purpuric spots or petechiae. The hair was gray and scanty. The fundi showed retinal pallor; the mucous membranes of the mouth were pale; the teeth were in fair condition, and the tonsils were atrophic. The thyroid was normal, and there was no adenopathy. The breasts were pendulous, the lungs clear and the heart not enlarged. The sounds were distant but of fair quality. A soft systolic murmur at the apex was not transmitted. The pulmonic second sound was normal, and the aortic second sound was not heard. The pulse was soft and regular, with a rate of 96. The abdomen was obese. The fundus was 6 cm. below the xiphoid process. The fetal heart rate was 130, heard in the left lower quadrant. The head was not engaged. The liver, spleen and kidneys were not palpable. There were no masses and no evidence of ascites. The extremities were normal. Neurologic examination gave negative results.




The solid line shows the hemoglobin content (grams per hundred cubic centimeters, Sahli) and the broken line the red blood cell count (millions per cubic millimeter).

A catheterized specimen of urine was amber, cloudy and acid, with a specific gravity of 1.016. Examination showed a trace of albumin, no sugar, acetone, diacetic acid or bile and a normal amount of urobilin. Microscopic examination showed an occasional granular cast and an occasional white blood cell and epithelial cell. Study of the blood showed hemoglobin content 3.5 Gm. (Sahli), red cells 1,300,000, color index 1 and white cells 5,000, with 80 per cent polymorphonuclears, 18 per cent lymphocytes and 2 per cent monocytes. The red cells stained deeply. Anisocytosis, macrocytosis, and polychromatophilia were observed. The polymorphonuclear neutrophils showed a shift to the right. The platelets appeared reduced. No parasites were seen. The Wassermann and Kahn reactions of the blood were negative. The nonprotein nitrogen content of the blood was 30 mg. per hundred cubic centimeters. The icteric index was 13. In the bromsulphalein test for hepatic function no dye was retained (negative reaction). The delayed direct Van den Bergh reaction was very faintly positive, and the indirect reaction was very faintly positive. The stool was brown and gave a negative reaction for occult blood, ova and parasites. An analysis of the gastric contents during fasting showed a free hydrochloric acid content of 10 degrees and a total acid content of 23 degrees. After the patient had taken 50 cc. of 7 per cent alcohol, analysis showed a free hydrochloric acid content of 40 degrees and a total acid content of 53 degrees. Tests were negative for blood, lactic acid and micro-organisms.

The patient was given three transfusions of citrated blood, totaling 1,200 cc., and received 3 cc. of liver extract intramuscularly every other day. Symptomatically she was much improved but her blood picture did not respond well, as shown in the accompanying chart. On the tenth day in the hospital vitamin B therapy in the form of two brewers' yeast tablets three times a day was started. On her eleventh day the membranes ruptured spontaneously, and after three hours of labor

she was delivered of a normal male infant weighing 6½ pounds (2,948 Gm.). She lost very little blood during delivery and there was no shock. Oxygen and ether were administered intermittently during labor and the delivery. On the second postpartum day the patient appeared tired and pale. Her pulse rate was 110 and the quality was rather poor at times. The blood picture showed a return to the level of admission. She was given another transfusion of 350 cc. of citrated blood and the following day appeared much improved. Liver extract was given every other day, and she received six brewers' yeast tablets daily. She made a rapid recovery and was discharged from the hospital on June 18.

The infant weighed 7 pounds 12 ounces (3,515 Gm.) on discharge. A blood count done on its fourth day showed the hemoglobin content 22.2 Gm. (Sahli), red cells 6,000,000, white cells 5,000 and differential count normal. On smear the red cells were seen to be uniformly large and deeply stained.

One year later the patient's blood picture was checked by Dr. E. R. Comstock and was found to be normal. She had had no complaints during the interval. No liver or vitamin therapy was used during this time.

### COMMENT

A search of the literature, including the work of authors from India,[1] New Zealand,[2] France,[3] South America,[4] Italy[5] and the United States[6] reveals some agreement on the treatment of this condition but marked differences of opinion on its cause. The incidence varies from one for 10,000 pregnancies in the temperate zones to twenty-nine for 1,000 pregnancies in India. The clinical picture is that of acute anemia developing during the third trimester of pregnancy. Pallor and extreme weakness are constant symptoms. A low grade fever occurs in 80 per cent of the cases. Vomiting and diarrhea are common; the latter is said to indicate a poor prognosis. Dyspnea and edema occur late. Paresthesias are often noted, but no definite lesions of the cord have been found. There may be glossitis, splenomegaly, hepatomegaly and occasionally purpura. A lemon-yellow color of the skin is uncommon. Laboratory examination shows severe hyperchromic anemia, the hemoglobin content usually being below 6 Gm. per hundred cubic centimeters, with a high color index. The blood chemistry is essentially normal. The stools show nothing of significance, although they may be watery and sometimes foamy. The urine usually contains a trace of albumin, rarely more than 0.5 per cent; casts in moderate numbers are observed. Urobilin is not present. Gastric acidity may be normal, reduced or absent. As to cause, no specific disease has been constantly associated with this condition. Many different theories have been advanced, but few have any concrete evidence for substantiation. Castle and Strauss[6] expressed the opinion that the mechanism of production is similar to that of true pernicious anemia. Wills[1] has shown that massive doses of liver extract will produce a reticulocyte response comparable to that of pernicious anemia, but she also found that vitamin B in the form of a yeast extract (marmite) was equally effective in producing regeneration of the blood.

Blood transfusion is the most important single item of treatment, as patients with this condition are desperately ill and may die of myocardial failure before a satisfactory response to liver or vitamin B therapy can be obtained. The mortality rate for untreated patients runs as high as 90 per cent, while with adequate treatment a mortality rate as low as 10 per cent can be obtained. Termination of pregnancy is generally agreed to be contraindicated. Efforts should be directed toward improving the patient's condition before she goes into labor. Iron, arsenic and vitamins A, C and D have been shown to be without value.

Fetal death in utero is common, but if the fetus lives until term the prognosis is good. The infant's blood picture is normal.

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2. Bennett, Francis: The Pernicious Anemia of Pregnancy, New Zealand M. J. 34:330 (Oct.) 1935.
3. Ionesco, V. T., and Sonciu, Olga: Contribution à l'étude de l'anémie pernicieuse gravidique, Sang 9:510-523, 1935. Alberti, Charles: Pernicious Anemia of Pregnancy (Presse méd. 43:1) 1935.
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## *Special Clinical Article*

# THE DIAGNOSIS AND TREATMENT OF WOUNDS OF THE HEART

### A REVIEW OF TWENTY-TWO CASES

### CLINICAL LECTURE AT SAN FRANCISCO SESSION

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Wounds of the heart demand early diagnosis and operation, for delay is rapidly fatal. Every attempt at accurate diagnosis should be made before operation, since exposure of the heart is in itself hazardous. The occasion for cardiorrhaphy arises rarely and always in cases in which immediate intervention is required; therefore the surgeon should have in mind the definite principles involved in the diagnosis and treatment. The object of this paper is to review twenty-two cases in which operation was performed and to set out certain principles based on that experience.

### GENERAL CONSIDERATIONS

*Incidence.*—Wounds of the heart are relatively rare. At the Medical College of Virginia Hospitals 0.1 per cent of surgical patients had such injuries,[1] and in my own experience[2] approximately 2 per cent of penetrating wounds of the chest injured the heart. Considering the size of the heart in relation to the chest and its exposed position, it is surprising that it is not more frequently injured. If patients who die of cardiac wounds but never reach the hospital were considered, the percentage would probably be much higher.

*Weapons Producing Wounds.*—All the patients in this series were Negroes. Wounds were produced either with a knife (fifteen cases) or an ice pick (seven cases). The type of knife is one generally referred to as a "switch blade," with a thin 4 inch blade. No patients with gunshot wounds of the heart have been treated, for the reason that they usually die from hemorrhage before reaching the hospital.

From the Department of Surgery, Emory University School of Medicine.

Read in the Surgical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Bigger, I. A.: Wounds of the Heart and Pericardium, South. M. J. 29:18 (Jan.) 1936.
2. Elkin, Daniel C.: Wounds of the Thoracic Viscera, J. A. M. A. 107:181 (July 18) 1936.

*Location of Wounds.*—The approximate location of the wounds is shown in the accompanying diagram. As is to be expected from the position of the heart in relation to the anterior wall of the chest, wounds of the right ventricle are more numerous; but wounds of all four chambers, as well as of the intrapericardial portion of the aorta (two cases) and pulmonary artery (one case), have been encountered. The location of the wound is of no importance so far as symptoms are concerned, and the exact position can only be surmised before operation, but it is of prognostic importance for reasons which will be mentioned later.

## DIAGNOSIS

*History.*—Symptoms are due to tamponade and loss of blood. The former is of great importance because of the narrow margin of safety under which the heart works. A rapid change in the pressure relationships of the heart affects its filling and emptying and thereby leads to cerebral anemia and death. All the patients in this series had tamponade of the heart, and in a majority of instances there was a history or evidence of external bleeding or blood was found in large quantities in the pleural cavity. Death may occur from hemorrhage without the establishment of tamponade, but I have not seen it do so.

The history is usually characteristic. Bleeding is profuse at first, with no other symptoms for several minutes. During this period the patient suffers no effects of the injury. One of my patients "ran three blocks," another "walked several hundred feet" and a third was able to "fight for about ten minutes." This phase is followed by exhaustion and collapse, frequently with unconsciousness. Occasionally a raving delirium (thought due to cerebral anemia) develops. At the same time there is usually a cessation of bleeding from the external wound. This chain of symptoms is due to gradually developing tamponade. When the heart is wounded it bleeds freely to the outside or into the pleural cavity. At the same time blood collects in the pericardial cavity. When from 100 to 200 cc. has collected the pericardium becomes distended, the intrapericardial pressure rises and the venae cavae can no longer empty normal quantities of blood into the heart. The heart, being unable to fill to capacity, can no longer empty, and cerebral anemia results.

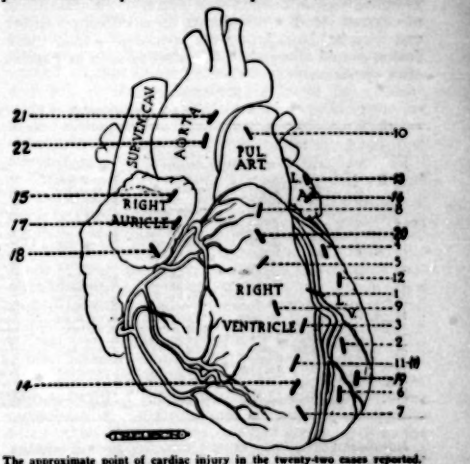
*Physical Appearances.*—The patient has usually been comatose or in a state of wild delirium when brought to the hospital. The position and direction of the external wound are of some importance in diagnosis, but the course of a knife thrust is notoriously misleading, although those just to the left of the sternum from the second to the fifth interspaces are most apt to injure the heart. Careful probing of the external wound may show by pulsation of the instrument that the heart is injured.

The skin is cold and moist. Because of the venous congestion, there is marked pallid cyanosis of the lips and tongue. The heart sounds are muffled and distant, and the pulse weak or absent.

*Arterial and Venous Pressure.*—The arterial pressure is lowered or unobtainable and the venous pressure is raised, as evidenced by the strutted prominent external jugular veins. The estimation of the venous pressure is of value in determining the extent of the tamponade and the progress of cardiac compression. A normal venous pressure is generally considered to range between 75 and 125 mm. of water. A pressure as high as 340 mm. has been seen and is consistent with life if not maintained for too long a period. The venous pressure rapidly drops with release of the tamponade, and the arterial pressure rises.[3] Readings of the venous pressure are of value after operation in cases in which the reaccumulation of blood or fluid is suspected in the pericardium. They should be made with the needle and manometer on a level with the heart and with the patient in a horizontal position.

*Roentgenographic Examination.*—Roentgenograms of the heart are of no value, since death may occur from an amount of blood too small to cause a noticeable change in the size and contour of the cardiac shadow.

Fluoroscopic examination, as pointed out by Bigger,[4] is of great value, since an accumulation of blood in the pericardial sac prevents normal pulsations. Of all the diagnostic methods this is the most accurate both in proving and in disproving one's suspicions of cardiac tamponade. It had best be done at the bedside with a portable fluoroscope, since moving the patient may increase the bleeding.




The approximate point of cardiac injury in the twenty-two cases reported.

*Electrocardiograms.*—These are of little value in establishing a diagnosis, since normal tracings may be obtained for several hours after an injury, but are of aid in determining the extent and progress of infarction after suture of the wound.[4]

*Summary.*—A lowered or falling arterial pressure, a high or rising venous pressure and the absence of cardiac pulsations by fluoroscopic examination make the diagnosis of tamponade practically certain. In the cases here presented the diagnosis was made before operation in each instance. No patient was needlessly subjected to operation.

## OPERATION

After a diagnosis is established, immediate operation should be carried out. Danger of infection and the frequent deaths from this cause demand the most

3. Elkin, Daniel C.: Wounds of the Heart, J. Thoracic Surg. 5: 390 (Aug.) 1936.
4. Elkin, D. C., and Phillips, Heywood: Stab Wound of the Heart; Electrocardiographic Studies of Two Cases, J. Thoracic Surg. 1: 113 (Dec.) 1931.

meticulous care in the preparation and the carrying out of the operation under a rigid aseptic technic. However, no time should be wasted, and for this reason the operating room should be set up as soon as the presence of a cardiac wound is suspected. In order to save time, all the instruments needed for an operation on the heart are kept in a separate container and sterilized by autoclave. While preparations are made for operation, the patient should be kept as quiet as possible by administration of morphine. External heat should be applied and the patient's head lowered. Infusion of saline solution, transfusion and measures which tend to raise the blood pressure are of little or no value if tamponade is present and may do harm in increasing the hemorrhage. The administration intravenously of a 6 per cent solution of acacia should be given when the operation is begun. Autotransfusion of citrated blood is of value as an emergency measure and may be done during the operation. Blood transfusion should always be performed as soon as possible after operation.

auricles or great vessels, the incision may be continued across the sternum and the pectoral muscles on both sides, retracted, and a portion of the sternum removed, if necessary for a proper approach to the wound. An excellent and inexpensive instrument for cutting the sternum is the ordinary blacksmith's horse-shoe clipper. A third method, and one giving excellent exposure, consists of turning a flap of skin and muscle laterally and removing two or more costal cartilages.

With any type of incision, the internal mammary vessels are ligated and divided, the triangularis sterni muscle is divided, and the lung and pleura are displaced outward by gauze dissection. If time permits, every effort should be made to avoid injuring the pleura, since the collapse of the lung adds greatly to the shock. The wound in the pericardium is then located and enlarged, or, if the wound is not readily found, the pericardium is opened between stay sutures. If tamponade exists, the pericardial wound is usually bleeding slightly, if at all, but when the intrapericardial pressure is released, bleeding becomes marked and the

TABLE 1.—*Summary of Twenty-Two Cases of Cardiac Wounds.*

| Case No. | Sex | Age | Instrument | Period from Duration to Admission | Location | Result | Cause of Death | Survival Period | Comment |
|---|---|---|---|---|---|---|---|---|---|
| 1 | ♂ | 18 | Knife | 30 minutes | R. ventricle | Recovery | ..... | ..... | Well 7 years |
| 2 | ♂ | 25 | Knife | 40 minutes | R. ventricle | Recovery | ..... | ..... | Well 6 years |
| 3 | ♂ | 41 | Knife | 30 minutes | R. ventricle | Death | Pericarditis | 3 days | Necropsy; wound healed |
| 4 | ♀ | 25 | Knife | "Few min." | L. ventricle | Death | Hemorrhage | None | Large wound; died on table |
| 5 | ♂ | 30 | Knife | ? | R. ventricle | Recovery | ..... | ..... | Well 4 years |
| 6 | ♂ | 20 | Knife | "Few min." | L. ventricle | Death | Pneumonia | 2 days | Necropsy; wound healed |
| 7 | ♂ | 21 | Knife | 30 minutes | R. ventricle | Recovery | ..... | ..... | Well 3 years |
| 8 | ♂ | 32 | Knife | Not known | R. ventricle | Death | Emphysema | 14 days | Mediastinal emphysema |
| 9 | ♀ | 27 | Knife | 60 minutes | R. ventricle | Recovery | ..... | ..... | Well 3 years |
| 10 | ♂ | 24 | Ice pick | Not known | Pul. artery | Death | Pneumonia | 2 days | Necropsy not done |
| 11 | ♂ | 34 | Knife | Not known | R. ventricle? | Recovery | ..... | ..... | Well 5 years |
| 12 | ♂ | 22 | Ice pick | Not known | L. ventricle | Death | Bacteremia | 36 hours | Necropsy; wound healed |
| 13 | ♀ | 36 | Ice pick | "Few min." | L. auricle | Recovery | ..... | ..... | Well 2 years |
| 14 | ♀ | 30 | Ice pick | "Few min." | R. ventricle | Recovery | ..... | ..... | Well 2 years |
| 15 | ♂ | 29 | Knife | 15 minutes | R. auricle | Recovery | ..... | ..... | Well 15 months |
| 16 | ♂ | 43 | Knife | Not known | L. auricle | Death | Hemorrhage | None | Died from hemorrhage at operation |
| 17 | ♂ | 36 | Knife | 30 minutes | R. auricle | Death | Infection | 3 days | Necropsy not done |
| 18 | ♂ | 22 | Knife | 1 hour ? | R. auricle | Death | Hemorrhage | None | Died from hemorrhage at operation |
| 19 | ♂ | 30 | Ice pick | Not known | L. ventricle | Death | Pneumonia | 2 days | Necropsy; wound healed; pneumonia |
| 20 | ♂ | 30 | Knife | Not known | R. ventricle | Recovery | ..... | ..... | Well 11 months |
| 21 | ♀ | 29 | Ice pick | "Few min." | Aorta | Recovery | ..... | ..... | Well 2 months |
| 22 | ♂ | .. | Ice pick | Not known | Aorta | Death | Pneumonia | 2 days | Necropsy not done |

Inhalation anesthesia is preferable for several reasons. The pleura may be accidentally opened during the operation or already opened by the wound, and nitrous oxide and oxygen under positive pressure is necessary for the inflation of the lung. When the tamponade of the heart is released there is usually a recovery of consciousness, and the patient will become excited, struggle and interfere with the procedure at the most inopportune time.

The incision should be planned to secure the best exposure in the quickest time and with the least shock. Some idea as to the position of the wound in the heart may be obtained from the position of the external wound, but the course of a stab wound is notoriously misleading. The medium sternotomy (Duval-Barasty) gives excellent exposure of the heart and the great vessels and by this approach the pleura is less likely to be opened. However, it requires a great deal of time, as does the closure of the wound, and is productive of shock. In the event of severe hemorrhage or increasing tamponade, the patient would not be likely to survive such a procedure.

The intercostochondral thoracotomy (Spangaro) offers a rapid approach to the heart but not a particularly good exposure. It can be enlarged by cutting or removing the cartilages above and below the incision and by removing a portion of the sternum. In wounds near the base of the heart or in those involving the contractions of the heart increase in force. With the release of the tamponade the arterial pressure rises and the venous pressure drops. The greatest difficulty in suturing the wound is in the placing of the first stitch. This is facilitated by removing the blood by suction and, when the wound is located, by placing the index finger of the left hand over it. By this method the flow of blood will be impeded sufficiently to allow the passage of a suture directly beneath the finger. This is left untied and is held in the left hand for traction and hemostasis. The wound can then be readily sutured and closed completely. Fine black silk on small full curved needles is the material of choice. The sutures should pass into the substance of the muscle but not into the chambers of the heart. This procedure is difficult in the thin-walled aorta and pulmonary artery or in the auricles, but suture material inside them is apt to be the starting point of a clot which may prove fatal. Wounds located in the edges of the heart, on its posterior surface or behind the sternum are best reached by placing an apex suture as advocated by Beck.[5] By this method the heart may be rotated and the wound brought into position. After control of the hemorrhage, the pericardium is cleansed of clots by flushing with physiologic solution of sodium chloride. The peri-

5. Beck, Claude S.: Wounds of the Heart, Arch. Surg. 13:203 (Aug.) 1926.

cardium is closed with interrupted sutures of silk, space being allowed for the drainage of fluid, which is sure to accumulate. The muscle, fascia and skin are closed carefully in layers without drainage.

### PROGNOSIS

The immediate prognosis depends largely on the interval between injury and operation. Delay may cause death from hemorrhage or tamponade or both. It likewise depends on the character and extent of the injury; a bullet usually causes two wounds, with greater hemorrhage and loss of tissue. The postoperative prognosis is dependent on infection, purulent pericarditis and pneumonia, as will be seen from the summary of cases (table 1). All except three patients survived the operation but died from complications in periods ranging from one to fourteen days (table 2).

Of the twenty-two patients, eleven died and eleven recovered. This mortality of 50 per cent is approximately the average for the cases reported in the literature up to this time. The percentage of recoveries is questionable because of the fact that many single cases with a favorable outcome have been reported, whereas those ending fatally are not so apt to be recorded.

The location of the wound is of prognostic importance. As will be seen from table 3, there were eight wounds of the right ventricle and six of the patients recovered. On the other hand, of the six patients with wounds of the left ventricle only two recovered. This is probably due to the fact that the operative approach to the right ventricle and the suture of this chamber are easier. Wounds of the auricles and of the intrapericardial portion of the aorta and pulmonary artery are more hazardous because of the difficulty of approach and because of the difficulties of suturing these thin-walled structures.

TABLE 2.—*Cause of Death*

| | Number Died |
|---|---|
| Hemorrhage | 3 |
| Pericarditis, infection | 3 |
| Pneumonia | 4 |
| Emphysema | 1 |
| Total | 11 |

TABLE 3.—*Location of Wound*

| | Total Patients | Recovered |
|---|---|---|
| Aorta (intrapericardial) | 2 | 1 |
| Pulmonary artery (intrapericardial) | 1 | 0 |
| Right auricle | 3 | 1 |
| Left auricle | 2 | 1 |
| Right ventricle | 8 | 6 |
| Left ventricle | 6 | 2 |
| Total | 22 | 11 |

### SUMMARY

The diagnosis of a wound of the heart can be made with practical certainty from the history, the arterial and venous pressure and the fluoroscopic examination.

The operative treatment should be carried out immediately.

The prognosis is dependent on the interval elapsing between the time of injury and the institution of treatment and on the postoperative complications, mainly infections. Wounds of the right ventricle offer a better prognosis.

50 Armstrong Street.

## Special Article

# HUMAN REQUIREMENTS OF VITAMIN C

SYBIL L. SMITH, A.M.

WASHINGTON, D. C.

*The following is the thirty-first and the concluding article in the present series on vitamins, published under the auspices of the Council on Foods and the Council on Pharmacy and Chemistry. This series of articles will be published in book form.*—ED.

It was early found that about twice as much vitamin C is required to prevent the first appearance of microscopic alterations in the teeth as to prevent the outward symptoms of scurvy in guinea pigs. It was also observed that in infants and children receiving enough vitamin C for protection against scurvy there may still develop a condition of latent or subacute scurvy accompanied by more or less severe injury to the teeth. It then became apparent that considerably larger quantities of vitamin C are required for good nutrition than for the prevention of scurvy.[1]

The first attempt at using human beings as subjects for the determination of requirements of vitamin C was made in Sweden in 1931 by Göthlin,[2] who measured the capillary resistance or fragility of two forcibly fed schizophrenic subjects during a period on a liquid diet which at first was devoid of vitamin C and later supplemented with increasing quantities of orange juice until the lowered capillary resistance was barely restored to normal. This point was reached on daily intakes of 0.7 and 1 cc. per kilogram of body weight respectively. Translated into modern terms, this would correspond to from 21 to 30 mg. of ascorbic acid for an adult weighing 60 Kg., or about 132 pounds. In Göthlin's opinion the disturbance in the strength of the capillaries as measured by his blood pressure method corresponds to the microscopic alterations in the teeth of guinea pigs as measured by the Höjer[3] tooth structure method, and by relating these two methods he concluded that a man weighing 60 Kg. requires from fourteen to twenty times as much vitamin C as a guinea pig weighing 300 Gm. for corresponding protection. When ascorbic acid became available Göthlin[4] used it in place of orange juice in this indirect method of determining human requirements with resulting values of from 19 to 27 mg. daily—quantities surprisingly close to the value of from 21 to 30 mg. calculated from the direct experiments on human subjects.

This indirect method, however, has received less attention since knowledge of the chemical identity of ascorbic acid has made possible more or less satisfactory tests for its identification, and its availability in quantity has led to its use in metabolic studies with determinations in the urine and blood subsequent to the ingestion or injection of known quantities of the vitamin. Following the now classic studies of Harris and his asso-

1. Sherman, H. C., and Smith, Sybil L.: The Vitamins, ed. 2, New York, Chemical Catalog Company, 1931, chapt. IV.
2. Göthlin, G. F.: A Method of Establishing the Vitamin C Standard and Requirement of Physically Healthy Individuals by Testing the Strength of Their Capillaries, Skandinav. Arch. f. Physiol. 63:225 (May) 1931.
3. Höjer, J. A.: Method for Determining the Anticorbutic Value of a Foodstuff by Means of Histological Examination of the Teeth of Young Guinea Pigs, Brit. J. Exper. Path. 7:356 (Dec.) 1926.
4. Göthlin, G. F.: Human Daily Requirements of Dietary Ascorbic Acid, Nature 134:569 (Oct. 13) 1934.

ciates,[5] Johnson and Zilva[6] and Hess and Benjamin[7] on the relation of urinary excretion to the intake of vitamin C as determined by indophenol titration, and of King and his associates,[8] Gabbe[9] and Farmer and Abt[10] on the significance of the concentration of ascorbic acid in blood as determined by the same indicator with certain modifications in technic, the outlook seemed encouraging toward the close of 1934 for the establishment of definite standards for judging vitamin C nutrition and requirements for various age groups. As is often the case, however, the problem has become more rather than less complicated with increased study. This is due chiefly to the fact that thus far no entirely specific method has been developed for the chemical determination of ascorbic acid. Among the numerous reports that have been published during the past three years there have been quite as many dealing with difficulties in methodology as with definite requirements. Brief mention of the more important sources of error in the determination of ascorbic acid in blood and urine has been given in a previous paper of the series.[11] Space does not permit the detailed discussion of methodology, which is almost necessary for the evaluation of data on which present recommendations of requirements are based. The problem is still further complicated by the multiplicity of methods that have been used to interpret data on metabolism in terms of quantitative requirements as reviewed in the following section.

## METHODS OF DETERMINING THE REQUIREMENTS OF VITAMIN C

The state of vitamin C nutrition in human beings is determined by one or more of three measurements: (1) the resistance or fragility of the blood capillaries, (2) the excretion of ascorbic acid in the urine and (3) the content of ascorbic acid in the fasting blood. To make use of these measurements for the estimation of requirements of vitamin C involves the acceptance of certain standards based on repeated observations on healthy normal persons.

*Capillary Resistance or Fragility.*—In this method the strength of the blood capillary system is measured on the upper arm by the positive pressure technic of Göthlin[12] or by the negative pressure technic of Dalldorf.[13] It was at first anticipated that this would prove to be a very practical method for survey work in estimating the vitamin C nutrition of large groups of people, but this has not proved to be the case, in this country at least. The literature on the use of the method has been reviewed recently in THE JOURNAL.[14] Since then, papers dealing with the usefulness and limitations of the method have appeared from the laboratories of both Göthlin and Dalldorf.

According to Göthlin,[15] the capillary fragility test serves as a measure of the physiologically indispensable minimum requirement of vitamin C, for it can be used to determine the quantity of the vitamin necessary to maintain the capillary system on the borderline between a normal and a weakened condition. The test is also useful in detecting a rather severe degree of vitamin C undernutrition. From simultaneous tests for capillary fragility and the determination of the ascorbic acid content of the fasting blood it has been shown that at this borderline of capillary strength the ascorbic acid content of the blood lies between 0.1 and 0.14 mg. per hundred cubic centimeters, values considerably below the generally accepted minimum normal value of about 0.6 mg. per hundred cubic centimeters. Consequently there is a degree of vitamin C deficiency within the range in ascorbic acid content of the blood of from 0.1 to 0.6 mg. which cannot be detected by the capillary fragility test. In Göthlin's opinion the reason the capillary fragility test is considered of little value as a means of detecting vitamin C undernutrition in certain countries, while in Sweden where his work has been done it has been found so satisfactory, is that in countries where there is an abundance of vitamin C-containing foods blood values seldom fall as low as 0.14 mg. per hundred cubic centimeters, and consequently there is no reaction with the capillary fragility test. In Sweden, however, during the long winter months the vitamin C content of the diet is so low that capillary fragility develops in thousands and the test is very useful as a means of detecting the most severe deficiencies.

A more clinical slant to the problem is given by Sloan from Dalldorf's hospital laboratory.[16] Applying the test with negative pressure technic to several normal subjects, two subjects with bleeding but no scorbutic symptoms and a fairly large group of patients with all degrees of scorbutic symptoms from simple bleeding of the gums to severe scurvy, he has concluded that the capillary resistance test in the majority of cases gives dependable information concerning the presence or absence of vitamin C depletion but does not indicate the degree of depletion and gives falsely negative results in the presence of severe anemia.

*Urinary Excretion of Ascorbic Acid.*—The twenty-four hour output of ascorbic acid in the urine as determined by indophenol titration according to various modifications of the original Tillmans method[17] has been used more generally than any other value as a measure of vitamin C nutrition and excretion after test doses as a means of calculating requirements. In the early work of Harris and his associates[18] the term "resting level" of vitamin C was used to indicate the day-by-day excretion of the vitamin, with a value of about 10 mg. representing the borderline between deficiency and adequacy, 20 mg. a moderately low intake and 40 mg. a liberal intake of the vitamin. Somewhat later, on finding that adult subjects on a daily intake of 25 mg. of ascorbic acid, selected as representing the "minimum-optimal" requirement, excreted about 13 mg.

5. Harris, L. J.; Ray, S. N., and Ward, A.: The Excretion of Vitamin C in Human Urine and Its Dependence on the Dietary Intake, Biochem. J. 27:2011, 1933.
6. Johnson, S. W., and Zilva, S. S.: The Urinary Excretion of Ascorbic and Dehydroascorbic Acids in Man, Biochem. J. 28:1393, 1934.
7. Hess, A. F., and Benjamin, Helen R.: Urinary Excretion of Vitamin C, Proc. Soc. Exper. Biol. & Med. 31:856 (April) 1934.
8. Yavorsky, M.; Almadon, Philip, and King, C. G.: The Vitamin C Content of Human Tissue, J. Biol. Chem. 106:525 (Sept.) 1934.
9. Gabbe, E.: Bestimmung von Vitamin C im Blutserum, Klin. Wchnschr. 13:1389 (Sept. 29) 1934.
10. Farmer, C. J., and Abt, A. F.: Ascorbic Acid Content of Blood, Proc. Soc. Exper. Biol. & Med. 32:1625 (June) 1935.
11. Bessey, O. A.: Vitamin C: Methods of Assay and Dietary Sources, J. A. M. A. 111:1290 (Oct. 1) 1938.
12. Göthlin, G. F.: Outline of a Method for the Determination of the Strength of the Skin Capillaries and the Indirect Estimation of the Individual Vitamin C Standard, J. Lab. & Clin. Med. 19:484 (Feb.) 1933.
13. Dalldorf, Gilbert: A Sensitive Test for Subclinical Scurvy in Man, Am. J. Dis. Child. 46:794 (Oct.) 1933. Dalldorf, Gilbert, and Russell, Hollis: The Effect of Cevitamic Acid Injections on Capillary Resistance, J. A. M. A. 104:1701 (May 11) 1935.
14. Youmans, J. B.: The Present Status of Vitamin Deficiencies in Practice, J. A. M. A. 108:15 (Jan. 2) 1937.
15. Göthlin, G. F.: When Is Capillary Fragility a Sign of Vitamin C Subnutrition in Man? Lancet 2:703 (Sept. 18) 1937.
16. Sloan, R. A.: A Comparison of Methods for Detecting and Grading Subclinical Scurvy, J. Lab. & Clin. Med. 23:1015 (July) 1938.
17. Tillmans, J.; Hirsch, P., and Hirsch, W.: Das Reduktionsvermögen pflanzlicher Lebensmittel und seine Beziehung zum Vitamin C: I. Der reduzierende Stoff des Citronensaftes, Ztschr. f. Untersuch. d. Lebensmitt. 63:1 (Jan.) 1932. Harris, Ray and Ward,[5] Bessey, O. A., and King, C. G.: The Distribution of Vitamin C in Plant and Animal Tissues and Its Determination, J. Biol. Chem. 103:687 (Dec.) 1933.
18. Abbasy, M. A.; Harris, L. J.; Ray, S. N., and Marrack, J. R.: Diagnosis of Vitamin C Subnutrition by Urine Analysis: Quantitative Data, Lancet 2:1399 (Dec. 21) 1935.

daily, the Harris group [19] concluded that if a subject excretes less than 13 mg. of ascorbic acid a day and fails to respond by a marked increase in excretion on the first or second day to a test dose of 700 mg. per 10 stone (140 pounds, 63.5 Kg.) of body weight, his diet has contained less than the reputed minimum-optimal quantity of vitamin C. This excretion value of 13 mg. a day is often used without further qualification as a standard of adequacy, but, since it represents an intake within the range of the physiologic minimum requirement established by Göthlin,[2] as noted earlier, it should be considered as indicating the borderline of adequacy rather than an optimum condition. According to van Eekelen,[20] a daily excretion of 40 mg. indicates that the subject is in a state of vitamin C saturation.

It has been recognized from the first that a better picture of vitamin C nutrition can be obtained by the so-called test dose or saturation method than by a determination of the resting level of excretion alone. Briefly, this method consists in determining the daily excretion during a period in which large doses of ascorbic acid are given to saturate the tissues. In the use of the method there has been little agreement as to general procedure and interpretation. Opinions differ as to the size of the test dose, the method of administration, the end point of saturation and the final calculation of the data.

A dosage of 700 mg. per 10 stone (140 pounds) of body weight, as first recommended by Harris and his associates,[19] has been used most frequently, although doses as low as 100 mg. and as high as 1,000 mg. have been reported. When the ascorbic acid is taken by mouth, as is commonly the case, the excretion of 50 per cent or more of the entire test dose within twenty-four hours, or of the half-day dose within twelve hours,[21] is commonly used as the criterion of saturation, although this will depend on the size of the test dose, for the larger the dose the lower the percentage excreted. This makes it difficult to compare observations of different investigators who have used test doses varying in size.

It has been shown that the peak of excretion of ascorbic acid in the urine occurs within from four to six hours following oral administration,[22] and within from one to three hours following intravenous administration.[23] Subcutaneous injection is preferred to intravenous by van Eekelen and Heinemann,[22] who consider that when the test dose is given intravenously the concentration in the blood is raised so suddenly that a transitory overflow into the urine results before the tissues are saturated. In their experience a test dose not exceeding 300 mg. when given subcutaneously to a saturated subject, is entirely excreted within six hours, with the peak occurring just before the end of the third hour. According to Baumann,[24] the best insight into the behavior of saturation is obtained by the oral administration over several days of small doses of ascorbic acid (50 mg. for small children, and 100 mg. for older children and adults). Under such conditions healthy persons excrete from 60 to 80 per cent of the test dose on the third or fourth day. He has noted a wide range in the saturation capacity of different persons as thus determined—the span ranging from 0 to 40 mg. of ascorbic acid per kilogram of body weight.

A difference has been shown recently in the behavior of various persons to continued administration of ascorbic acid after the saturation point has been reached, as shown by a sudden and marked increase in excretion of ascorbic acid. Instead of additional increases with continued high doses, as might be expected if a real state of saturation had been reached, Hamel [25] found in some instances no further rise for several days. This plateau of excretion, indicating a disappearance of ascorbic acid after the body reservoirs had been filled, he attributed to a form of specific dynamic action, which should be taken into consideration in estimating requirements by the test dose method.

As a qualitative survey method for determining the state of vitamin C nutrition of large groups of subjects, the test dose method in its simplest form is undoubtedly of some value, as will be shown later. Advantage has been taken of the time interval before the peak of excretion has been reached after oral administration of the test dose to shorten the period of collection of urine in routine surveys of school children.[26] In the application of the method to the determination of the extent of vitamin C undernutrition of any age group, various procedures have been followed. The total quantity of ascorbic acid required before saturation is reached is sometimes referred to as the "saturation deficit," and the extent of this deficit is considered an index of the nutritional status of the subject with respect to vitamin C.[27] The number of days required to reach saturation on a given test dose serves as another index.[21] If a prolonged period on a vitamin C free diet precedes the saturation tests, the difference between intake and excretion up to the point of saturation is considered to be a measure of the maximum tissue reserves of the subject.[28]

Of the various procedures that have been developed for the application of the test dose method to the determination of actual requirements of vitamin C, two or three will be described in some detail as representative of methods designed to determine vitamin C requirements ranging from minimum to maximum or representing barely adequate to presumably optimal nutrition. At the lower end of the scale may be considered a method developed by Widenbauer [29] and used in an extensive investigation of human requirements. In a preliminary period of several days, during which the subject is kept on a uniform diet containing very little vitamin C, the titration value of the urine is determined

19. Harris, L. J.; Abbasy, M. A., and Yudkin, J.: Vitamins in Human Nutrition: Vitamin-C Reserves of Subjects of the Voluntary Hospital Class, Lancet 1:1488 (June 27) 1936.

20. van Eekelen, Marie; Emmerie, Adrianus, and Wolff, L. K.: Ueber die Diagnostik der Hypovitaminosen A und C durch die Bestimmung dieser Vitamine im Blut, Ztschr. f. Vitaminforsch. 6:150 (April) 1937.

21. Jezler, A., and Kapp, H.: Zur Frage des Vitamin C-Defizits, Ztschr. f. klin. Med. 130:178 (June 10) 1936.

22. Hawley, Estelle E., and Stephens, D. J.: Rate of Urinary Excretion of Test Doses of Ascorbic Acid, Proc. Soc. Exper. Biol. & Med. 34:854 (June) 1936. van Eekelen, Marie, and Heinemann, M.: Critical Remarks on the Determination of Urinary Excretion of Ascorbic Acid, J. Clin. Investigation 17:293 (May) 1938.

23. Hawley and Stephens.[22] Ralli, Elaine P.; Friedman, G. J., and Kashow, M.: An Excretory Test for Vitamin C Deficiency and Subnutrition, Proc. Soc. Exper. Biol. & Med. 36:52 (Feb.) 1937. Wright, I. S.; Lillenfeld, Alfred, and MacLeanthes, Elizabeth: Determination of Vitamin C Saturation: A Five Hour Test After an Intravenous Test Dose, Arch. Int. Med. 60:264 (Aug.) 1937. Faulkner, J. M., and Taylor, F. H. L.: Observations on the Renal Threshold for Ascorbic Acid in Urine, J. Clin. Investigation 17:69 (Jan.) 1938.

24. Baumann, T.: Die Bestimmung der physiologischen Spanne der C-Vitamin Sättigung des Organismus, Klin. Wchnschr. 16:1246 (Sept. 4) 1937.

25. Hamel, P.: Ueber die Vitamin C-Bilanz des Menschen: II. Beinahesättigungsversuche zur Bestimmung des täglichen Verbrauches und des Sättigungsdefizits, Klin. Wchnschr. 16:1105 (Aug. 7) 1937.

26. Harris, L. J., and Abbasy, M. A.: Nutrition Surveys: A Simplified Procedure for the Vitamin-C Urine Test, Lancet 2:1429 (Dec. 18) 1937.

27. Gander, J., and Niederberger, W.: Ueber den Vitamin C-Bedarf aber Leute, München. med. Wchnschr. 83:1387 (Aug. 21) 1936.

28. O'Hara, Patricia H., and Hauck, Hazel M.: Storage of Vitamin C by Normal Adults Following a Period of Low Intake, J. Nutrition 12:413 (Oct. 10) 1936.

29. Widenbauer, F.: Der Vitamin C Haushalt des Menschen unter verschiedenen Verhältnissen, Klin. Wchnschr. 16:600 (April 24) 1937.

by the Harris and Ray method[8] on two twelve hour samples preserved with 10 per cent glacial acetic acid, and the average daily value thus obtained is considered as a blank to be deducted from the final average excretion. Test doses of from 200 to 500 mg. of ascorbic acid per day are then administered orally until saturation is reached, as shown by an excretion of at least 50 per cent of the half-day dose in twelve hours. Then follows a period of adjustment of the daily dose of ascorbic acid to the quantity required to give a titration value slightly higher than the preliminary blank value. When this dosage has been established, the same quantity is given over a final period of seven days with daily titrations of the urine to determine the average daily excretion value. The final calculation of requirement is made by subtracting from the average daily intake during the final period the average daily excretion in the same period minus the average daily excretion of the preliminary period. As the values thus obtained represent a bare equilibrium between intake and output, they may be considered as minimum requirements providing for no margin of safety.

The scheme followed by van Eekelen and her associates[30] consists essentially in first saturating the subject on a daily dose of 250 mg. of ascorbic acid, then depleting the reserves by a period of several weeks on a vitamin C free diet, and finally saturating again as in the first period, the end point in both being a sudden and marked increase in excretion. The total intake of ascorbic acid in the second saturation period divided by the number of days before saturation is considered as the daily use or actual requirement. Since the final period is one of saturation rather than of bare equilibrium, the values obtained represent more liberal allowances than those of Widenbauer. The method has been criticized, however,[31] as giving entirely different results, depending on the length of the intermediate depletion period, a point which will be discussed later.

A somewhat different procedure for determining maximum or optimal requirements but also depending on saturation tests has been developed by Hauck.[32] Briefly, this consists in first saturating the tissues by daily intakes of 200 mg. of ascorbic acid for six days—a period found long enough with the subjects studied to insure complete saturation as determined by the increase in excretion following a single test dose of 400 mg. The entire test is repeated two or three times to establish the individual response to the 400 mg. dose when saturation is complete. Finally a series of similar tests is run on graded doses of ascorbic acid until the least quantity is found which will induce a similar response to the test dose of 400 mg. as obtained in the preliminary tests. With the provision made in this method for complete saturation of the tissues and for individual standards of comparison, the values obtained may be considered to represent maximum requirements.

*Concentration of Ascorbic Acid in the Blood.*—The content of reduced ascorbic acid in fasting blood of normal subjects does not vary with age but within certain limits is dependent on previous dietary intake of vitamin C. In the data reported in the literature[33] there appears to be rather closer agreement as to the lower than the higher limits of normality, the range extending from a minimum of about 0.6 mg. to a maximum of from 1.5 to 2 mg. or more per hundred cubic centimeters.

Abt and Farmer[34] have stated that "the cevitamic acid (reduced) content of the blood varies directly with the vitamin C content of the previous diet." In the opinion of Greenberg, Rinehart and Phatak,[33a]

> the estimation of the reduced plasma ascorbic acid is only a measure of the immediate nutritive or metabolic level relative to vitamin C, and is dependent on recent dietary habits to a large degree. Although it is an index of the vitamin C nutrition at the time of the test, in a single case a low level does not imply tissue injury or scurvy (either clinical or subclinical). The latter results from the operation of suboptimal or low metabolic levels over some period of time. Conversely, a good or high level would not indicate that deficiency had not operated to produce tissue injury in the past. A more accurate index of the degree of deficiency existing at the time in any given case can be had by means of serial determinations following administration of known vitamin C supplements.

Portnoy and Wilkinson[35] have observed occasional subnormal plasma values in subjects showing no other test for vitamin C deficiency and have suggested a similar explanation. In their opinion, however,

> the finding of a normal or high plasma ascorbic acid shows the patient to have good reserves of the vitamin (always assuming that a large dose of vitamin C-containing food has not been taken before the test begins) and a single estimation should be sufficient without corroborative evidence from other tests.

*Relationship Between the Ascorbic Acid Content of Blood and Urine.*—A straight line relationship between the initial ascorbic acid content of the blood and the total quantity of ascorbic acid required for saturation as determined by excretion in the urine was demonstrated by van Eekelen and her associates,[30] who showed that with an ascorbic acid content of the blood of about 0.4 mg. per hundred cubic centimeters a total of 2 Gm. of ascorbic acid was required before saturation was reached as compared with only 1 Gm. for an initial blood value of 0.8 mg. per hundred cubic centimeters. They consider that the degree of vitamin C saturation of a subject can be estimated simply by a single blood determination in place of the tedious urinary excretion tests, a blood content of from 0 to 0.4 mg. of ascorbic acid per hundred cubic centimeters denoting a poor, from 0.4 to 0.8 mg. a moderate, from 0.8 to 1.2 mg. a very good and above 1.2 mg. an excellent state of saturation. A similar relationship was noted by Baumann,[24] who found that with blood values as low as 0.45 mg. per hundred cubic centimeters from 20 to 40 mg. of ascorbic acid per kilogram of body weight was required

30. van Eekelen, Marie: On the Metabolism of Ascorbic Acid (Vitamin C), Acta brev. Neerland. **8**:165 (Dec. 14) 1935. van Eekelen, Marie; Heinemann, M., and van Wersch, H. J.: On the Daily Requirements for Ascorbic Acid of Man, ibid. **6**:107 (June 20) 1936. van Eekelen, Marie: On the Amount of Ascorbic Acid in Blood and Urine: The Daily Human Requirement for Ascorbic Acid, Biochem. J. **30**:2291 (Dec.) 1936.

31. Göthlin, G. F.; Frisell, E., and Rundquist, N.: Experimental Determinations of the Indispensable Requirements of Vitamin C (Ascorbic Acid) of the Physically Healthy Adult, Acta med. Scandinav. **92**:1 (June 6) 1937.

32. Hauck, Hazel M.: Unpublished data.

33. (a) Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cevitamic (Ascorbic) Acid Determinations in Blood Plasma and Their Relationship to Capillary Resistance, J. Pediat. **8**:1 (Jan.) 1936. (b) Taylor, F. H. L.; Chase, D., and Faulkner, J. M.: The Estimation of Reduced Ascorbic Acid in Blood Serum and Plasma, Biochem. J. **30**:1119 (July) 1936. (c) Deggeller, J. C.: Researches on the Vitamin C Content of the Blood, Acta brev. Neerland. **6**:64 (July 4) 1936. (d) Stephens, D. J., and Hawley, Estelle E.: The Partition of Reduced Ascorbic Acid in Blood, J. Biol. Chem. **115**:653 (Oct.) 1936. (e) Greenberg, L. D.; Rinehart, J. F., and Phatak, N. M.: Studies on Reduced Ascorbic Acid Content of the Blood Plasma, Proc. Soc. Exper. Biol. & Med. **35**:135 (Oct.) 1936. (f) Ingalls, T. H.: Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, J. Pediat. **10**:577 (May) 1937. (g) Pijoan, M., and Eddy, E.: Ascorbic Acid Content of Red Cells and Plasma, J. Lab. & Clin. Med. **22**:1227 (Sept.) 1937. (h) Baumann.[24] (i) Sloan.[29]

34. Abt, A. F., and Farmer, C. J.: Cevitamic Acid Content of the Blood Plasma, Am. J. Dis. Child. **54**:682 (Sept.) 1937.

35. Portnoy, B., and Wilkinson, J. F.: Vitamin C Deficiency in Peptic Ulceration and Hematemesis, Brit. M. J. **1**:554 (March 12) 1938.

for saturation, whereas a content of over 1.4 mg. per hundred cubic centimeters indicated a high degree of saturation.

Evidence leading to the conclusion that ascorbic acid has a definite renal threshold value at a blood concentration of about 1.4 mg. per hundred cubic centimeters has been reported by Faulkner and Taylor [23] with the conclusion that blood values at or above this level indicate saturation and below this level unsaturation in varying degree. Others believe that the threshold value varies with the person [36] and more particularly that there are two types of persons with high and low threshold values respectively.[37] This would account for the wide span which has been noted in the saturation capacity of different individuals.[38] Neuweiler's [37] evidence in support of this hypothesis is of interest also in indicating when it is safe to use blood values alone as a measure of saturation. Among the forty-three nonpregnant women whom he studied, all but one out of twelve with initial blood values ranging from 1 to 1.5 mg. per hundred cubic centimeters came within the normal four day limit of saturation, according to the Jezler and Kapp method,[21] while all five subjects with blood values under 0.6 mg. per hundred cubic centimeters required from six to eight days to complete the test.

The remaining twenty-seven subjects with blood values decreasing from 0.95 to 0.6 mg. per hundred cubic centimeters gave inconsistent results, some completing the test within four days while others with the same initial blood values required a longer time. Neuweiler concluded that while both high and low blood values may furnish sufficient evidence of the vitamin C nutrition of a person, intermediate values of from about 0.6 to 1 mg. per hundred cubic centimeters should not be considered alone but in connection with the results of saturation tests.

Oral and intravenous tolerance tests involving simultaneous determinations of the blood and urine at frequent intervals following the administration of a single massive dose of ascorbic acid orally or intravenously have been recommended by Portnoy and Wilkinson [35] as furnishing the most reliable information concerning the state of vitamin C nutrition. Individual variations in the rate of absorption of ascorbic acid from the intestinal tract or possible destruction of the vitamin are considered to render the oral test somewhat less satisfactory than the intravenous tolerance test. It is suggested that in the latter method, when used as a routine, blood tests may be omitted and determinations made only of the ascorbic acid excretion during the first five hours following the injection. This abbreviated test, however, may not be valid in cases of damage to the kidneys, which is revealed by simultaneous tests on the blood and urine.[39]

### REQUIREMENTS OF VARIOUS AGE GROUPS

*Infants.*—The vitamin C reserves of the infant at birth depend on the state of nutrition of the mother, with umbilical cord blood usually giving higher values than the corresponding maternal venous blood,[40] possibly because of increased use of the vitamin by the mother during labor. In a group of twenty-two hospitalized cases, Braestrup [41] obtained average values of 0.26 mg. of ascorbic acid per hundred cubic centimeters for the maternal blood, 1.07 mg. for the cord blood and 0.69 mg. for capillary heel blood of the infants thirty minutes after birth. Ten days after birth these capillary blood values had dropped to an average of 0.27 mg. per hundred cubic centimeters. The mothers in this study had been on diets very deficient in vitamin C before admission to the hospital, which may account for the low value of the maternal blood.

The rapid decrease in ascorbic acid content of the blood during the first ten days, as noted, suggests that the reserves with which the infant is supplied at birth are sufficient for only a few days and that thereafter vitamin C must be supplied either through breast milk or as a supplement to artificial feeding in order to maintain the blood concentration at the level which seems indicative of a good vitamin C reserve at any age. Mindlin [42] reports an average plasma ascorbic acid value of 1 mg. per hundred cubic centimeters for a group of about twenty infants at the age of 2 weeks, as compared with 0.3 mg. for a comparable group artificially fed from birth or for at least six days before the test, and from 0.4 to 0.8 mg. for a smaller group of artificially fed infants receiving 20, 30 or 75 mg. of ascorbic acid for a week or more, the 20 mg. dose giving as good results as the larger amounts. Braestrup [41] also found that initially low blood levels could be raised to from 0.56 to 0.76 mg. per hundred cubic centimeters by a 20 mg. supplement of ascorbic acid daily but were not affected by 10 mg. These data, although fragmentary, suggest that to maintain the ascorbic acid content of the blood of artificially fed infants at low normal values during the first weeks of life not less than 20 mg. of ascorbic acid daily is needed. In Braestrup's subjects, whose weights were given, this allowance is equivalent to from 5 to 6 mg. per kilogram of body weight.

On the basis of estimates of the vitamin C intakes of breast-fed and artificially fed infants from 9 to 12 days of age excreting in twenty-four hours more than 50 per cent of test doses of 30 mg. of ascorbic acid per kilogram of body weight, injected subcutaneously, Neuweiler [43] also arrived at the conclusion that the vitamin C requirement of very young infants is in the vicinity of 6 mg. per kilogram of body weight and concluded that the diet of infants, especially the artificially fed, should be supplemented at this early age (less than 2 weeks) with fruit juices or a pure preparation of ascorbic acid.

In view of the fact that formerly it was considered unnecessary to supplement the diet of artificially fed infants with vitamin C before the age of 3 or 4 months and that the most recent (December 1937) recommendation of the Technical Committee on Nutrition of the

36. Lund, H.: Eine quantitative und spezifische Methode zur Ascorbinsaurebestimmung im Harn und zur Bestimmung des Schwellenwertes, Klin. Wchnschr. **16**:1083 (July 31) 1937.
37. Wachholder, K., and Hamel, P.: Ueber die Vitamin C-Bilanz des Menschen: III. Täglicher Bedarf und Güte des Versorgungszustandes nach den Beziehungen des Blutgehaltes zu Ausscheidung und Gewebssättigung, Klin. Wchnschr. **16**:1740 (Dec. 11) 1937. Neuweiler, W.: Ueber den Nachweis des Vitamin C-Sättigungsgraden des Organismus, Ztschr. Vitaminforsch. **7**:128, 1938.
38. Baumann,[b] Hamel.[a]
39. Wright, I. S., and MacLenathan, Elizabeth: Vitamin C Saturation—Kidney Retention After an Intravenous Test Dose of Ascorbic Acid, Proc. Soc. Exper. Biol. & Med. **38**:55 (Feb.) 1938.
40. Abt, Farmer and Epstein.[40a] Wahren, H., and Rundquist, O.: Ueber den Ascorbinsäuregehalt des Blutes von Mutter und Frucht, Klin. Wchnschr. **16**:1498 (Oct. 23) 1937. Braestrup, F. W.: Studies of Latent Scurvy in Infants: 1. Capillary Resistance of Newly-Born Children and During the First Year of Life; 2. Content of Ascorbic (Cevitamic) Acid in the Blood-Serum of Women in Labour and in Children at Birth, Acta paediat. **19**:320, 328, 1937. Nielsen, H. E.: Serumascorbinsyren under Normale og Forskellige Pathologiske Forhold, Bibliot. f. læger. **130**:20 (Jan.) 1938.
41. Braestrup, F. W.: Studies of Latent Scurvy in Infants: III. The Content of Reduced Ascorbic Acid in Blood Plasma in Infants, Especially at Birth and in the First Days of Life, J. Nutrition **16**:363 (Oct.) 1938.
42. Mindlin, R. L.: The Relation Between Plasma Ascorbic Acid Concentration and Diet in the Newborn Infant, J. Pediat. **13**:309 (Sept.) 1938.
43. Neuweiler, W.: Vitamin C—Stoffwechsel bei Neugeborene, Ztschr. f. Vitaminforsch. **6**:75 (Jan.) 1937.

Health Organization of the League of Nations [44] for the vitamin C requirement of artificially fed infants is from 5 to 15 mg. a day, what other evidence is at hand to prove or disprove this more generous allowance at an earlier age?

A condition of subacute vitamin C deficiency has been recognized [45] as occurring occasionally in infants as early as the second day of life. The condition is described as a vague nutritional upset with disturbance in water metabolism and excessive loss in weight responding promptly to treatment with ascorbic acid. Ley conducted urinary excretion tests on four male infants 4 days of age, two of whom (one breast-fed and one artificially fed) showed these symptoms of vitamin C deficiency. Although the absolute values reported are probably of no great significance, it is of interest that the excretion of ascorbic acid of the two normal infants was about twice that of the other two. The artificially fed infant was then given 50 mg. and the mother of the breast-fed infant 300 mg. of ascorbic acid daily, following which both infants showed marked clinical improvement. The urine tested after ten or twelve days had increased in volume and ascorbic acid content, and the ascorbic acid content of the breast milk had increased from 3.57 to 6.07 mg. per hundred cubic centimeters. From these and other observations, Ley concluded that there is a wide variation in the vitamin C needs of individual infants during the first few weeks of life, owing to differences in functional capacity and the oxidation processes of intermediary metabolism.

From analyses by the customary indophenol titration method of tissues and organs of infants dying at birth or at varying intervals up to the age of 4 months, Ingalls [46] has shown progressive exhaustion of vitamin C reserves with increasing age. Even more convincing evidence of the effects of lack of vitamin C in this early period of life was shown by Ingalls in the case histories and histologic sections of the bones and costochondral junctions of a small group of premature infants receiving only pasteurized mother's milk and dying before the age of 4 months. These showed unmistakable signs of vitamin C deficiency not detected during life. Accordingly, Ingalls feels that some source of vitamin C should be given as early as the first week in life. "This is particularly important for premature infants, for the artificially-fed and for those suffering from disease."

Szent-Györgi [47] once made the statement "ein optimal funktionierender Körper kann nicht durch Vitamin zufuhr verbessert werden." Later in illustrating this principle he [48] showed that while a laboratory guinea pig may be kept in a presumably satisfactory and healthy condition and be protected from outward symptoms of vitamin C deficiency on from 1.5 to 2 mg. of ascorbic acid, it requires a much larger dose for protection against diphtheria and other bacterial toxins, and in its own natural environment may consume from 20 to 40 mg. of ascorbic acid daily from green food. This quantity also represents the dose required for complete saturation of the animal's tissues. In his opinion, in the long run the physiologic quantity of any vitamin will be found to be the amount which in its original environment the organism in question consumes daily. Applied to the vitamin C requirements of infants, this might be construed to mean the quantity of ascorbic acid furnished by the day's supply of breast milk of the best quality.

Breast milk has long been considered much richer than cow's milk in vitamin C. Chemical tests have confirmed this belief but have shown fairly wide variations in content, depending largely on the food supply of the lactating woman. (Requirements for lactation will be discussed later.) However, the range in concentration and average values reported by investigators in different countries using similar methods of titration with 2,6 dichlorophenolindophenol are surprisingly uniform.[49] The values taken as a whole show that breast milk from women on satisfactory diets may be expected to furnish from 4 to 7 or 8 mg. per hundred cubic centimeters during the first few months of lactation. In fact, a concentration below 4 mg. per hundred cubic centimeters has been considered [50] to indicate a vitamin C deficiency in the tissues of the lactating woman.

Estimates of the daily consumption of vitamin C by breast-fed infants vary according to the values selected as most representative of the average concentration of the vitamin in breast milk. Selleg and King [49d] have estimated that under optimal conditions with a fluid intake of 21 ounces (630 cc.) an infant may receive as much as from 40 to 50 mg. of ascorbic acid daily from breast milk during the first few weeks. Widenbauer [51] has reported values ranging from 18 to 78 mg. in the twenty-four hour supply of breast milk from wet nurses in different stages of lactation and at the height of saturation by the test dose method. The highest values under these conditions are, naturally, not representative of the ordinary content of ascorbic acid in breast milk. Ingalls,[46] using 4 mg. per hundred cubic centimeters as an average value, has estimated that the normal infant during the first three months of life, in consuming from 500 to 1,000 cc. of breast milk, receives the equivalent of from 20 to 40 mg. of ascorbic acid daily. Braestrup [41] considers that with an average milk consumption of 150 cc. per kilogram of body weight a breast-fed infant may receive a minimum of 3 mg. and a maximum of 8 mg. of ascorbic acid per kilogram of body weight daily during the first few months of life.

None of these calculated intakes from breast milk of good quality fall below and most of them are considerably above the estimated requirements reviewed and far above the 1937 recommendation of the League of Nations Committee, as previously noted.

In spite of differences in the methods which have been used in estimating the vitamin C requirements of infants, the recommended allowances fall within the comparatively narrow range of from 5 to 8 mg. of ascorbic acid per kilogram of body weight or from 20 to 50 mg. daily after the first few days. These requirements may be met, during the first few months, by breast feeding alone under optimal conditions. How-

44. Report by Technical Commission on Nutrition on Work of the Third Session, Bull. Health Organ., League Nations 7:475, 1938.

45. Ley, L.: Die Bedeutung des Vitamin C für das Neugeborene, Klin. Wchnschr. 10:1425 (Oct. 9) 1937.

46. Ingalls, T. H.: Ascorbic Acid Requirements in Early Infancy, New England J. Med. 218:872 (May 26) 1938.

47. Szent-Györgi, Albert: Die medizinische Bedeutung des Vitamins C, Deutsche med. Wchnschr. 60:356 (April 13) 1934.

48. Szent-Györgi, Albert: Les propriétés thérapeutiques des vitamines, Presse méd. 51:599 (June 25) 1938.

49. (a) Neuweiler, W.: Ueber den Gehalt der Frauenmilch an Vitamin C, Ztschr. f. Vitaminforsch. 4:39 (Jan.) 1935. (b) Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin-C Subnutrition by Urine Analysis, with a Note on the Antiscorbutic Value of Human Milk, Lancet 1:71 (Jan. 12) 1935. (c) Wachholder, K.: Die Versorgung des Säuglings mit Vitamin C, Klin. Wchnschr. 15:193 (April 23) 1936. (d) Selleg, Iva, and King, C. G.: The Vitamin C Content of Human Milk and Its Variation with Diet, J. Nutrition 11:599 (June) 1936. (e) Widenbauer, F., and Kühner, A.: Ascorbinsäurestudien an stillenden Frauen, Ztschr. f. Vitaminforsch. 6:50 (Jan.) 1937.

50. Baumann, T., and Rappolt, L.: Untersuchungen zum C-Vitaminstoffwechsel: II. Ueber die C-Vitaminausscheidung und den C-Vitaminbedarf laktierender Frauen, Ztschr. f. Vitaminforsch. 6:8 (Jan.) 1937.

51. Widenbauer, F.: Der Vitamin C-Haushalt stillender Mütter, Ernährung 2:64 (Feb.) 1937.

ever, it may be safer and more economical to supply some of the vitamin C directly to the infant rather than rely entirely on breast feeding. This practice is even more necessary for infants receiving pooled mother's milk instead of breast feeding. A 27 per cent loss of ascorbic acid was reported for samples of mother's milk held in a refrigerator for eighteen hours,[49d] and samples of pasteurized pooled mother's milk as delivered to a hospital from a directory for mother's milk were found to contain only 0.3 mg. of ascorbic acid per hundred cubic centimeters or less than one tenth as much as fresh breast milk of average quality.[49e]

The ascorbic acid content of cow's milk ranges from 1 to about 2.6 mg. per hundred cubic centimeters for raw and from 0.4 to 1 mg. for pasteurized milk.[52] The probable extent of reduction of these initial low values by the time the milk is ready for consumption by the artificially fed infant has been shown by Hawley [53] in analyses for ascorbic acid of samples of milk as taken from various delivery wagons to a city health bureau laboratory for bacteriologic count.

The raw milk sampled had an average ascorbic acid content of 1.65 mg., the pasteurized milk 0.9 mg. and formulas prepared from the milk for use in the hospital nursery 0.61 mg. per hundred cubic centimeters.

According to Hawley, "if non-glass cooking utensils are used in the home, even further reduction is probable. As a result the average formula of the infant (600-750 cc.) would supply only 4 to 6 mg. of vitamin C and cannot, therefore, be considered an adequate source of this vitamin."

These figures for breast milk, pooled mother's milk, and cow's milk, as modified for infant feeding, afford rather convincing evidence of the advisability of furnishing supplementary sources of vitamin C to all infants at a very early age, the need increasing from breast-fed infants to those receiving milk mixtures.

The reluctance of some physicians to recommend vitamin C supplements at an earlier age and in more generous quantities than formerly may be due in part to hesitation to apply to vitamin C the doctrine of the newer knowledge of nutrition with its distinction between the terms "adequate" and "optimal." Possibly an infant protected against the earliest detectable sign of capillary fragility may be thought to be receiving adequate vitamin C. To the physician formerly accustomed to seeing many cases of unmistakable infantile scurvy, protection against scurvy may even indicate an adequate provision of the vitamin but in neither case can the state of nutrition be considered optimal if there are no reserves to meet unexpected demands—no margin of safety.

Probably the best indication of whether or not the individual infant's need of vitamin C is being fully met is by determinations of the reduced ascorbic acid content of the blood plasma. According to Ingalls,[48] reduced values of ascorbic acid in the plasma from 2 to 1 mg. per hundred cubic centimeters indicate complete saturation, from 1 to 0.7 mg. normal, from 0.7 to 0.5 mg. low normal, from 0.5 to 0.3 mg. suboptimal, from 0.3 to 0.15 mg. asymptomatic scurvy and from 0.15 mg. to 0 scurvy. On the basis of combined saturation and blood tests conducted on a group of healthy infants and children, Chu and Sung [54] have proposed a similar classification based on ascorbic acid values on the plasma as follows: deficiency stage 0.17-0.41 mg., presaturation 0.54-0.8 mg., relative saturation 0.86-1.36 mg., and postsaturation 0.85-1.25 mg. These figures are in good agreement with the standard proposed by Ingalls, based on blood values alone. It will be seen that the lowest values, 0.15 and 0.17 mg. per hundred cubic centimeters, correspond to the blood content above which, according to Göthlin, the test for capillary fragility is inapplicable. Between this "physiological minimum" and the theoretic optimal is a fairly wide range with a still indefinite end point. In Ingall's opinion "it would seem logical to suppose that saturation is the truly optimal state of ascorbic acid nutrition for the infant since in the event of an increased demand or decreased supply the vitamin depot is presumably larger than in partial saturation."

Acceptance of the theory of saturation as the optimal state involves the selection of maximum rather than minimum estimates of requirements of vitamin C. Ordinarily the additional needs of the breast-fed infant and the entire needs of the artificially fed can be met by daily allowances of orange juice, tomato juice or other fruit juices without resorting to ascorbic acid, which, however, is extremely useful in cases in which fruit juices are poorly tolerated. Of particular value to the physician or hospital dietitian in calculating the equivalent quantities of various fruit juices in terms of the day's requirement of vitamin C is the recent report of the Council on Foods [55] on the ascorbic acid content of all brands of commercially canned fruit juices accepted by the Council prior to Sept. 1, 1937. With fresh orange juice of an average ascorbic acid content of about 0.5 mg. per cubic centimenter, a 50 mg. requirement would be met by 100 cc. of the juice. In comparison with this, equivalent volumes for the various canned juices studied were: canned orange juice 110 cc., lemon juice 100 cc., grapefruit juice 125 cc., tomato juice 250 cc. and pineapple juice 350 cc. These figures are only approximate and represent a rather wide range in individual values. Furthermore, the discovery of marked differences in the ascorbic acid content of varieties and strains of tomatoes [56] may be expected to raise the average of the vitamin C content of tomato juice through the selection for the commercial manufacture of tomato juice from strains of the highest vitamin C content. At present, however, it is safe practice to use the foregoing equivalents in making a substitution for orange juice in infant feeding. In large clinics with suitable laboratory facilities an even better practice, already adopted in some hospitals, is to determine the vitamin C content of each new supply of canned fruit juices for the necessary calculations in dietary prescriptions. A study of the relative costs of various fruit juices, canned and fresh, has been reported by Hawley.[57]

*Children.*—There have been very few reports of quantitative studies on the vitamin C requirements of healthy children. This is not surprising considering the difficulty in carrying out urinary excretion studies and the possible dangers involved in subjecting children to

52. Daniel, Esther P., and Munsell, Hazel E.: Vitamin Content of Foods, U. S. Dept. Agr., miscellaneous publication 275, June 1937, p. 175.
53. Hawley, Estelle E.: Vitamin C Content of Milks: Raw, Pasteurized and Baby Formulas, J. Am. Dietet. A. 14:275 (April) 1938.
54. Chu, F. T., and Sung, C.: The Vitamin C Content of the Blood Plasma in Normal and Sick Children, Chinese M. J. 51:791 (Dec.) 1937.
55. The Vitamin C Content of Commercially Canned Tomato Juice and Other Fruit Juices as Determined by Chemical Titration, Council on Foods, J. A. M. A. 110:650 (Feb. 26) 1938.
56. Macline, W. A.; Fellers, C. R., and Buck, R. K.: Tomato Variety and Strain Differences in Ascorbic Acid (Vitamin C) Content, Proc. Am. Soc. Hort. Sc. 34:343 (April) 1937. Tripp, Francis; Satterfield, G. H., and Holmes, A. D.: Varietal Differences in the Vitamin C (Ascorbic Acid) Content of Tomatoes, J. Home Econ. 29:258 (April) 1937.
57. Hawley, Estelle E.: The Vitamin C Content of Fruit Juices, J. Am. Dietet. A. 13:261 (Sept.) 1937.

the depletion in reserves involved in any of the test dose methods for determining requirements.

Among the subjects studied by Widenbauer,[29] using an elaborate procedure, was a healthy boy in his third year. In four out of seven tests his adjusted vitamin C consumption amounted to 22 mg., and in the other three to 21 mg. daily. These values are of special interest in terms of relative requirements, for by exactly the same methods the requirements of a grown man were 28 mg. in five tests, and 26 and 27 mg. in one test each. The very slight difference between the young child and the adult indicates that the vitamin C requirements throughout life cannot be calculated in terms of body weight alone, as was at one time suggested.[18]

In view of the customary use of cod liver oil or other vitamin A preparations in conjunction with orange juice in infant and child feeding, further observations on the same child are of interest. Immediately following the test period in which the consumption value of 21 mg. was established, he was given 2 tablespoonfuls of cod liver oil daily for two weeks, at the end of which time the values remained unchanged. Six months later, after a value of 22 mg. had been established, 5 cc. of the vitamin A concentrate "Vogan" was given daily for a week, after which a new test gave a value of only 9 mg. daily. These observations, which were substantiated on other subjects, suggest that vitamin A preparations at least do not increase the requirement of vitamin C and in particularly concentrated form may exert an indirect sparing action.

Three boys of preschool age (39, 57 and 59 months of age at the beginning of the experiment) served as subjects in what is perhaps the most detailed investigation of the vitamin C metabolism of young children thus far published in this country.[58] During twelve successive five day periods these children, who were kept under constant observation, were given weighed diets differing from period to period only in increasing and known amounts of vitamin C. With increasing intakes per kilogram of body weight the ascorbic acid retentions (intake minus output) were greater up to a certain point, beyond which there was no further increase with larger doses. The peaks in retention were reached at intakes of 7.5, 6.6 and 6.4 mg. per kilogram of body weight for the three subjects in the order of increasing weight. Retention values in two periods on these intakes were practically identical, 4.2, 3.8 and 3.6 and 4.1, 3.7 and 3.6 mg. per kilogram of body weight respectively. The somewhat higher intake and retention of the youngest child and the lower and almost identical values for the two older subjects are of interest in view of the difference of eighteen months between the ages of the youngest and next older, and only two months between this and the oldest child. If saturation is the criterion of optimal vitamin C nutrition, the intakes required for maximum retention might be considered as representing the vitamin C requirement of these children. Expressed as total daily intakes at the peak of retention, the average values in round numbers were 117, 121 and 120 mg. respectively. At this point the urinary excretion of vitamin C by two of the subjects exceeded and of the other very nearly equaled 50 per cent of the intake, another criterion of saturation.

There is a wide range between the Widenbauer figures of 20 and 21 mg. of ascorbic acid as the daily requirement of a child in his third year and the maximum retention or saturation values of from 117 to 123 mg. for children from 3 to 5 years of age, as calculated from these data of Everson and Daniels. Although the higher values seem unpractical if considered in terms of orange juice alone, 2 cc. of which is usually required to furnish 1 mg. of ascorbic acid, a considerable proportion of the total intake of ascorbic acid in these experiments was furnished by other foods—as would be the case in ordinary, well planned diets for growing children. In the particular diets on which maximum retentions were secured on the two extremes of intake, 116.7 and 122.8 mg. respectively, orange juice furnished 96 and 90 mg. of the total, requiring about 6½ and 6 ounces (195 and 180 cc.) respectively. While this is a considerably larger volume than the customary allowance for children, it is evidently not beyond the capacity of the preschool child.

Other studies dealing with the vitamin C metabolism of children [59] represent, for the most part, hospitalized patients and are of doubtful value in an estimation of the requirements of normal healthy children although of interest in showing the increased use or wastage of vitamin C in certain diseases.

The studies of Abt, Farmer and Epstein [32a] and of Ingalls [32f] have shown the constancy of the ascorbic acid content of blood plasma of normal subjects at different ages and the validity of applying to children the standards previously noted. Attention has already been called to the shortened procedure recommended by Harris and Abbasy [26] for routine surveys of school children. In attempting to set up a "normal minimal" standard of urinary output of ascorbic acid more adapted to children than the 13 mg. standard of Harris, Bumbalo [60] found that the excretion was directly dependent on the intake and showed no constancy from subject to subject. Among sixteen healthy children from 5 to 13 years of age, the twenty-four hour ascorbic acid excretion ranged from 11 mg. for a boy aged 13 years whose daily diet included a glass of orange juice (about 60 cc.) to 71 mg. for a girl aged 5 years consuming four or five large oranges daily. The average daily excretion for the group was approximately 28 mg. as compared with about 8 mg. for the same number of tuberculous children in the same age range. Baumann and Rappolt [61] consider that a child is in a state of vitamin C saturation if more than 80 per cent of a test dose of 100 mg. of acorbic acid administered orally is excreted within twenty-four hours; if the excretion is between 80 and 40 per cent, a slight deficiency, and under 40 per cent a marked deficiency is indicated.

Accumulated observations by these methods and further studies of the concentration of ascorbic acid in the blood of children on diets of known ascorbic acid content should afford a better basis for estimating the vitamin C requirements of children. Meantime the chief and perhaps the only valid arguments against great liberality in vitamin C allowances for young chil-

58. Everson, Gladys J., and Daniels, Amy L.: Vitamin C Studies with Children of Preschool Age, J. Nutrition 12:15 (July 10) 1936.

59. Harris, Abbasy and Yudkin.[29] Sendroy, J., Jr., and Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever: I. Quantitative Index of Ascorbic Acid Utilization in Human Beings and Its Application to the Study of Rheumatic Fever, J. Clin. Investigation 15:369 (July) 1936. Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever: II. Test of Prophylactic and Therapeutic Action of Ascorbic Acid, ibid. 15:385 (July) 1936. Abbasy, M. A.; Hill, N. G., and Harris, L. J.: Vitamin C and Juvenile Rheumatism, with Some Observations on the Vitamin-C Reserves in Surgical Tuberculosis, Lancet 2:1413 (Dec. 12) 1936. Abbasy, M. A.; Harris, L. J., and Gray Hill, N.: Excretion of Vitamin C in Osteomyelitis, ibid. 2:177 (July 24) 1937. Keith, J. D., and Hickmans, Evelyn M.: Vitamin C Excretion in Children with Particular Reference to Rheumatic Fever, Arch. Dis. Child. 12:125 (June) 1938.

60. Bumbalo, T. S.: Urinary Output of Vitamin C of Normal and of Sick Children, Am. J. Dis. Child. 55:1212 (June) 1938.

61. Baumann, T., and Rappolt, L.: Untersuchungen zum C-Vitaminstoffwechsel: 3. Ueber den C-Vitaminstoffwechsel bei Kindern, Ztschr. Vitaminforsch. 6:24 (Jan.) 1937.

dren are the relatively high cost of orange juice and equivalent quantities of tomato juice and other fruit juices, and the possible, although exceptional, danger of acquiring a sensitivity to these juices through unusually high intakes. For older children with a greatly increased variety of foods furnishing appreciable quantities of vitamin C it is possible to provide a liberal amount of the vitamin even in low cost diets. As a final word in favor of liberal allowances, a statement by Chapin [62] at a round table discussion at the 1937 meeting of the American Academy of Pediatrics may be quoted: "Apparently the minimum amount [of vitamin C] needed to prevent scurvy is only a fraction of the desired amount for optimal health. So far as is known, it has never been possible to produce toxic symptoms by giving large doses of vitamin C."

*Adults.*—Göthlin's earliest investigation of the physiologically indispensable requirements of vitamin C, as determined by tests for capillary fragility [2] has been repeated by Göthlin and his associates [31] with the use of ascorbic acid in place of orange juice and a mixed diet estimated to furnish only 2 mg. of ascorbic acid per person daily in place of the liquid diet of the earlier study. The subjects were again physically healthy schizophrenic adults, two males and two females, having normal gastric secretion of hydrochloric acid, blood sedimentation rate and capillary resistance. The experiment required from six to eight months for completion. At the point of final restoration to normal of the lowered capillary resistance the intakes of ascorbic acid, corrected by the addition of 2 mg. for the ascorbic acid content of the diet amounted to 0.39, 0.43, 0.44 and 0.48 mg. per kilogram of body weight for the four subjects respectively, representing a range of from 23.4 to 28.8 mg. for the total daily requirement of an adult weighing 60 Kg. These values are in surprisingly close agreement with the earlier estimates of from 21 to 30 mg. as calculated from the orange juice required in Göthlin's first experiments and of from 19 to 27 mg. as estimated from guinea pig requirements for the same degree of protection. Commenting on these values as related to dietary recommendations, the authors state:

> It will be realized that the daily supply should be more generous than the figures indicate. The supply should no more be limited to what has proved to be the indispensable minimum than the supply of protein in the dietary for man should be limited to the minimum intake sufficient to maintain nitrogen balance.

However, no estimate is given for the lower limit of optimal daily intake on the ground that any investigation of this question

> should take into consideration the circumstance that the supply of vitamin C which has been usual for generations is, owing to differences in obtainable food material and consequently in diet, entirely different for the people who live in different latitudes, a circumstance which may also possibly have affected their vitamin requirements.

It is significant that by an entirely different method, but one which may also be interpreted as yielding minimum rather than optimal values, Widenbauer [29] obtained values of about 28 mg. as his own daily requirement over a total period of 210 days and that of a nonpregnant woman. As no account was taken of the vitamin C content of the diet, which was low but not absolutely free from ascorbic acid, the actual consumption of vitamin C was undoubtedly somewhat higher than the figures given.

In experiments conducted by van Eekelen [30] on herself following the method previously outlined, which may be expected to give higher values than either the Göthlin or the Widenbauer method, the requirement or "daily use" of ascorbic acid amounted to 34 mg. after a depletion period of ninety-four days and to 63 mg. after a period of only twenty-seven days. In van Eekelen's opinion, the daily requirement of ascorbic acid is adapted to the existing storage of the vitamin. If the diet is customarily low in vitamin C or if, as in the case of some of her experiments, there has been a prolonged depletion period, the requirement or "daily use" of the vitamin is lower than if the diet has been richer in the vitamin or there has been only a short depletion period. The selection of the upper value (63 mg.) as her daily requirement was presumably based on a consideration of her customary dietary habits. The same idea of decreased requirements with prolonged subsistence on diets low in vitamin C has been brought out by Wachholder,[63] who also considers it unwise to recommend the lowest values that may be obtained because they provide no margin of safety for increased use of the vitamin in infections and for the possible increased requirements of muscular work either in manual labor or in exhaustive sports.

With due recognition of the influence of the past dietary history on vitamin C requirements, a factor also recognized by Göthlin as already noted, the van Eekelen method still seems lacking in precision. Göthlin [31] has criticized the indefiniteness in the end point of the test as follows:

> Without an objective reason for deciding the duration of the period of abstinence, it appears that every preconceived view as to the requirements of ascorbic acid in man could find confirmation by means of an investigation in accordance with van Eekelen's principle provided that the length of the period of abstinence is adapted to suit the preconceived view.

In two other studies by essentially the same method [64] requirement values were obtained for four adult subjects equivalent to 0.70, 0.78, 0.83 and 0.83 mg. respectively per kilogram of body weight. For the adult weighing 60 Kg. the range in total daily requirement is from 42 to 50 mg., or nearly twice as much as the indispensable minimum requirement, whether determined by the Göthlin test for capillary fragility or by the saturation method of Widenbauer.

The saturation method employed by Hauck has not yet been tested on a sufficient number of subjects to warrant definite conclusions, but preliminary results are of considerable interest. For the six subjects (college graduate students and faculty) on whom at least three separate preliminary saturation tests had been made at the time of writing, the average responses in urinary excretion of ascorbic acid to a 400 mg. test dose administered after the subjects had received 200 mg. of ascorbic acid daily for six days in addition to the vitamin C furnished by a diet not absolutely free from vitamin C ranged from 229 to 274 mg. with two of the

62. Chapin, H. D.: Vitamins C and D (in Round Table Discussion on Vitamins), J. Pediat. **12**: 529 (April) 1938.

63. Wachholder, K.: Ueber die Vitamin C-Bilanz des Menschen: IV. Einschränkung des Bedarfes bei mangelhafter Zufuhr und deren ernährungsphysiologische Bedeutung, Klin. Wchnschr. **17**: 5 (Jan. 1) 1938.

64. van Wersch, H. J.: Determinations of the Daily Requirements for Ascorbic Acid of Man, Acta brev. neerland. **6**: 86 (July 4) 1936. Heinemann, M.: On Human Requirements for Vitamin C Under Different Conditions, ibid. **6**: 144 (Oct. 13) 1936. Heinemann, M.: I. On the Relation Between Diet and Urinary Output of Thiosulfate (and Ascorbic Acid): II. Human Requirements for Vitamin C, Biochem. J. **30**: 2299 (Dec.) 1936.

subjects giving no individual response above 249 mg. and two none lower than 240 mg. These values afford another illustration of differences in the saturation or retention capacities of different individuals. In four subjects for whom fairly clearcut results were obtained in the final adjustment in dosage of ascorbic acid to the smallest amount producing excretion values comparable to the individual standards established in the preliminary tests, the estimated requirements were equivalent to 1.18, 1.24, 1.33 and 1.62 mg. per kilogram of body weight or from a little over 70 to nearly 100 mg. as the daily requirement for maintaining complete saturation in an adult weighing 60 Kg.

Thus for adults as well as for infants and children the range of estimated requirements from the physiologically indispensable minimum to complete saturation is extremely wide—from 25 or 30 mg. to 100 mg. daily or from about 0.4 to 1.6 mg. per kilogram of body weight—a fourfold increase from the absolute minimum to what might be called luxus consumption. Whatever may be the uncertainty about the upper limits of requirement, there seems no doubt that the requirement of 30 mg., as adopted by the Technical Commission on Nutrition of the Health Organization of the League of Nations,[64] should be considered only as the minimum for protection against scurvy and not as the requirement for satisfactory nutrition. For this even the frequently recommended allowance of 50 mg. should probably be considered as the barely adequate rather than the optimal requirement, with considerably larger quantities desirable when economically possible. There is some indication that a particularly generous margin of safety should be the rule in allowances of vitamin C for old people.[65] As will be noted in the following section, pregnant and lactating women should have at least twice as much vitamin C as would meet the ordinary requirements of nonpregnant women.

A report from the Massachusetts and Rhode Island state colleges [66] covers urinary excretion studies on more than 200 freshmen and forty junior women students. The Massachusetts subjects included two groups of about seventy students each tested at the beginning and near the close of their first year at college and the Rhode Island subjects about sixty freshmen and forty juniors tested the same year. The range in the "resting level" of urinary ascorbic acid was very wide in each group but strikingly similar for the three groups of freshmen students as reflected in the graphic array of individual figures and also in values of 15 mg. (Rhode Island), 20 mg. (Massachusetts, 1936) and 22 mg. (Massachusetts, 1937) representing the average daily excretion of ascorbic acid of the subjects in each group. Corresponding averages for the Rhode Island juniors and practically the same groups of Massachusetts students tested in the spring of their freshman year were 28, 33 and 27 mg. respectively. These higher averages as well as decidedly higher values for some of the individual students suggest aroused interest in the selection of foods of higher intake of vitamin C as the result of individual or group instruction.

In the first period in the aforementioned study about 70 per cent of the Massachusetts and 85 per cent of the Rhode Island students had excretion values of 20 mg. or less, while in the second period this figure dropped to 46 and 47 per cent for the Massachusetts subjects and 50 per cent for the Rhode Island juniors. Unpublished data from comparable studies with even greater uniformity in technic on groups of students at the state colleges of Montana, Oregon, Washington and Utah [67] show a similar wide range in individual values. Rough calculations indicate that excretion values of 20 mg. or less were the rule in about 33 per cent of the Montana, 35 per cent of the Oregon, 30 per cent of the Utah and 32 per cent of the Washington group. If there is any significance in the statement of the Harris group [19] that an excretion of 20 mg. indicates a moderately low intake of vitamin C, it would seem that about one third of the young women college students in the Northwest and about three fourths of similar students in the Northeast with no particular dietary instruction were on a none too liberal vitamin C intake.

In these cooperative studies smaller numbers of subjects are being given saturation tests, and an effort is also being made to correlate the estimated vitamin C content of the individual diets with the excretion values, but informaton is not yet available on these points.

*Pregnant and Lactating Women.*—All evidence points to a greatly increased need of vitamin C in pregnancy, which continues through the lactation period. In the investigation of Widenbauer,[29] to which frequent reference has been made because of the comparative value of his data, a nonpregnant woman with a minimum requirement or "daily use" of 28 mg. was found to need 71 mg. in the third and 67 mg. in the eighth month of pregnancy. The slight drop in the later period may not be significant, but the two values in comparison with the nonpregnant value indicate a more than doubled requirement during pregnancy. Following the same method with a group of healthy women in the eighth and ninth months of pregnancy, Gaehtgens [68] obtained the rather wide range in values of from 33 to 64 mg. and recommended not less than 100 mg. daily as a safe requirement for pregnancy. As his values were obtained by a method which gives only about 28 mg. as the ordinary adult requirement, the additional allowance for pregnancy is very generous. In Gaehtgens' opinion, the increased vitamin C requirement during pregnancy is due not to increased metabolism but to the fetal and placental requirements for storage. Evidence of increased requirements during pregnancy has also been shown by Neuweiler [69] in urinary excretion tests following the intravenous injection of 200 mg. of ascorbic acid. More than half of a group of apparently healthy pregnant women were found by Gaehtgens and Werner [70] to have a significant saturation deficit as indicated by the increased length of time required for saturation according to the Jezler and Kapp criteria.[21]

It is obvious that the nursing mother needs enough vitamin C to meet her own requirements and to maintain a satisfactory concentration of the vitamin in her milk. The various studies on the requirements of vitamin C during lactation [71] have shown that under favor-

65. Harris, Abbasy and Yudkin.[19] Gander and Niederberger.[52]
66. Mitchell, Helen S.; Merriam, Orrena A., and Batchelder, Esther L.: The Vitamin C Status of College Women as Determined by Urinary Excretion, J. Home Econ., to be published.

67. Richardson, Jessie E.; Fincke, Margaret L.; Todhunter, E. Neige, and Brown, Almeda P.: Personal communications to the author.
68. Gaehtgens, G.: Der Tagesverbrauch an Vitamin C in der Schwangerschaft, Arch. f. Gynäk. 164:571 (Aug. 26) 1937.
69. Neuweiler, W.: Ueber den Bedarf an Vitamin C während Gravidität und Lactation, Klin. Wchnschr. 14:1793 (Dec. 14) 1935.
70. (a) Gaehtgens, G., and Werner, E.: Das Vitamin C-Defizit in der Gravidität, Arch. f. Gynäk. 165:473 (March 5) 1937; (b) Zur Frage des Vitamin C-Defizits in der Gravidität und während der Lactation, Klin. Wchnschr. 16:843 (June 12) 1937.
71. Neuweiler.[69] Chu, F. T., and Sung, C.: Effect of Vitamin C Administration on Vitamin C of Milk and Urine of Lactating Mothers, Proc. Soc. Exper. Biol. & Med. 35:171 (Oct.) 1936. Widenbauer and Kühner.[29a] Baumann and Rappolt.[29] Gaehtgens and Werner.[70b]

able conditions breast milk can be enriched to values considerably above the average but that there is an upper limit which cannot be exceeded. As Baumann [72] has expressed it, there is no lower threshold for the secretion of ascorbic acid from the blood into the milk and the process may go on until the maternal organism is greatly depleted, but there is an upper limit of concentration at about 8 mg. per hundred cubic centimeters of milk. Conversely, there is no upper limit of excretion of ascorbic acid in the urine but a lower one of about 0.1 to 0.14 mg. per hundred cubic centimeters of blood. Baumann and Rappolt [50] have calculated that for a milk production of 800 cc. a day with an ascorbic acid content of at least 5 mg. per hundred cubic centimeters at least 50 mg. of ascorbic acid should be added to the daily requirement of the nonpregnant woman.

A distinction has been pointed out by Gaehtgens and Werner [73] between the effects of a deficiency of vitamin C in pregnancy and in lactation. When the requirements are not met during gestation, the maternal organism becomes depleted at the expense of the fetus; whereas in lactation the maternal organism is protected and the infant suffers through decreased content of ascorbic acid in the milk. If this theory is sound, it would seem advisable to be more insistent on recommending a greatly increased intake of vitamin C during pregnancy than in lactation and rely more in the latter period on supplementing the probable deficiencies in the breast milk by giving orange juice or other easily taken and readily assimilable sources of vitamin C directly to the infant at a very early age. However, no harm and undoubtedly much benefit will accrue to the nursing mother if her vitamin allowance is doubled during the period of considerable drain on her reserves.

## FACTORS AFFECTING REQUIREMENTS OF VITAMIN C

While it is beyond the scope of this paper to discuss the requirements of vitamin C in illness, and the studies that have been reviewed in an attempt to arrive at some decision concerning requirements have been confined to those dealing with presumably physiologically healthy subjects, no greater argument can be given in support of liberality in allowances than to call attention to the increased use or disappearance of ascorbic acid which has been observed under various conditions of heightened metabolic activity such as heavy manual labor or violent exercise [28] and in certain febrile conditions, notably tuberculosis.[74] In fact it has even been suggested that ascorbic acid metabolism may be an index of total metabolism and thus serve as a general diagnostic guide.

## VITAMIN C IN HUMAN DIETS

With the ascorbic acid content of any individual food in its natural state varying as widely as has been shown in two recent critical compilations of the literature,[75] and with the uncertain losses that may occur in such foods before their final consumption, it has seemed useless to attempt to estimate requirements from records of food consumed by groups of presumably healthy persons of different ages, nor can such records be expected to give accurate data as to the actual consumption of ascorbic acid in comparison with estimated requirements. It is, nevertheless, of some interest, as indicating trends in consumption, to study the accompanying table, a companion to the one presented for vitamin A in a previous paper of this series.[76]. With all due allowance for the sources of error in such calculations, it is of significance that as the weekly expenditure for food increased the estimated ascorbic acid content of the diet increased almost without exception. When it is considered that in the low cost diets the proportion of ascorbic acid furnished by orange juice was probably much less than in diets of higher cost and that consequently a greater deduction should be made for losses of the vitamin before consumption, it will be seen that certainly the lowest cost diet, and probably the next higher (except for the farm group) furnished less than a safe allowance of vitamin C and that only in the two highest cost groups could the intake be considered to represent a very generous allowance.

*Estimated Ascorbic Acid Content of Diets of Families Not on Relief, 1935-1936 (in Milligrams per Requirement Unit)* *

| Region and Degree of Urbanization | Average† in Milligrams per Adult per Day‡ for Families Spending§ Weekly per Head for Food | | | | |
|---|---|---|---|---|---|
| | $1.25-$1.87 | $1.88-$2.49 | $2.50-$3.12 | $3.13-$3.74 | $3.75-$4.37 |
| City‖ | | | | | |
| North Atlantic | 40.0 | 57.5 | 70.0 | 87.5 | 97.5 |
| East North Central | 47.5 | 57.5 | 75.0 | 77.5 | 107.5 |
| East South Central | 50.0 | 67.5 | 85.0 | .... | .... |
| Pacific | 70.0 | 77.5 | 95.0 | 107.5 | 115.0 |
| Village# | | | | | |
| North Central | 40.0 | 57.5 | 77.5 | 77.5 | .... |
| Southeast | 40.0 | 52.5 | 72.5 | 95.0 | 92.5 |
| Pacific | 50.0 | 77.5 | 87.5 | 105.0 | 105.0 |
| Farm¶ | | | | | |
| North Central | 66.5 | 70.0 | 80.0 | 100.0 | .... |
| Southeast | 55.0 | 70.0 | 80.0 | .... | .... |
| Pacific | .... | 82.5 | 105.0 | .... | .... |

* Data furnished by Dr. Hazel K. Stiebeling, Senior Food Economist, Bureau of Home Economics, U. S. Department of Agriculture.

† These averages represent the value of the uncooked food. They are higher, therefore, than the value of food actually eaten.

‡ The following scale of family coefficients was employed in evaluating the ascorbic acid intake for families of different types in terms of an adult:

| | |
|---|---|
| Adults, 20 years and over | 1.0 |
| Boys 16-19 years | 1.2 |
| Boys 13-15 years | 1.0 |
| Boys 11-12 years, girls 14-19 years | 0.9 |
| Boys 9-10 years, girls 11-13 years | 0.8 |
| Boys 6-8 years, girls 4-10 years | 0.7 |
| Children under 4 years | 0.7 |

§ Adjusted to 1935 retail price levels.

‖ Families of employed workers. Field work conducted by the U. S. Bureau of Labor Statistics.

# All occupational groups.

¶ Farm operators; farm-furnished food valued at farm prices.

A point of interest is the consistently higher ascorbic acid content of the diets at all cost levels in the Pacific than in the North Atlantic region for the city families, the only group for which data are reported for both of these regions. These differences are brought out even more strikingly in the detailed report on the diets of families of employed wage earners and clerical workers in cities.[77] As many as 45 per cent of these families in the North Atlantic region bought foods supplying less than 37.5 mg. of ascorbic acid per requirement unit a day, whereas none of the Pacific city families had diets

72. Baumann, T.: Untersuchungen über den C-Vitaminstoffwechsel bei laktierenden Frauen und über den Grad der physiologischen und pathologischen C-Vitaminaufspeicherung des menschlichen Organismus, Jahrb. f. Kinderh. 150:193, 1937; Nutrition Abstr. & Rev. 7:1083, 1937.

73. Gaehtgens, G., and Werner, E.: Vitamin C-Belastungen bei Stillenden Wöchnerinnen, Arch. f. Gynäk. 165:63, 1937.

74. Martin, G. J., and Helse, F. H.: Vitamin C Nutrition in Pulmonary Tuberculosis, Am. J. Digest. Dis. & Nutrition 4:360 (Aug.) 1937.

75. Daniel and Munsell[66] Boas Fixsen, Margaret A., and Roscoe, Margaret H.: Tables of the Vitamin Content of Human and Animal Foods, Nutrition Abstr. & Rev. 7:823 (April) 1938.

76. Booher, Lela E.: Vitamin A Requirements and Practical Recommendations for Vitamin A Intake, J. A. M. A. 110:1920 (June 4) 1938.

77. Stiebeling, Hazel K., and Phipard, Esther F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, U. S. Dept. Agr. Circ. 507, 1939.

so low in vitamin C. With expenditures for food ranging from $2.50 to $3.12 per person weekly, considered representative of the moderately well-to-do, about 37 per cent of the families in the North Atlantic group and 70 per cent in the Pacific group bought food furnishing more than 75 mg. of ascorbic acid (uncorrected) a day. These figures are entirely consistent with the urinary excretion data for groups of college women in these areas for, as noted earlier, low excretion values for ascorbic acid (presumably indicative of low intake) were the case in from 75 to 80 per cent of the North Atlantic group and from 30 to 35 per cent in the Pacific group.

### SUMMARY AND CONCLUSIONS

A positive statement of human requirements is difficult to make because of uncertain or unsatisfactory methods for its determination in the living organism, lack of agreement as to the most satisfactory state of nutrition with respect to this vitamin and individual differences in requirements.

Based on the methods that have been followed, three levels of requirement may be considered in terms of the minimum quantities of ascorbic acid required: (1) to prevent the slightest decrease in capillary resistance or to maintain uniform excretion of the vitamin barely above that on a vitamin C-free diet; (2) to maintain uniform excretion after a depletion period following a preliminary saturation period, and (3) to maintain the tissues in a state of saturation as determined by various modifications of the test dose method. These levels of requirement may conveniently be termed the physiologically indispensable, adequate, and saturation or luxus consumption values respectively.

The estimated requirements for various age groups as reviewed lie within the following limits of absolute values: infants, from about 8 mg. (newly born) to 50 mg. daily; children, from 22 to 100 mg. or more; adults, from 28 to 100 mg. or more. With due allowance for unlike methods followed in their determination, these values may be considered to represent roughly the range from the physiologically indispensable minimum to saturation or luxus consumption. Values of about 20 mg. daily for infants, 40 mg. for children and from 50 to 60 mg. for adults may be considered as tentative estimates for the middle or barely adequate consumption level, with but little margin of safety or allowance for individual variations in requirement.

Requirements have also been estimated in terms of body weight: infants from 3 to 8 mg., children from 6.4 to 7.5 mg. and adults from 0.7 to 1.6 mg. per kilogram of body weight. While the data are far too incomplete to warrant separation of these values into the three levels or to permit of definite conclusions concerning the rate of decrease in requirement per unit weight with increasing age, a comparison of the absolute and relative values for different ages suggests that vitamin C requirements are related both to body weight and to metabolic rate, the effect of the latter being the more pronounced.

It has been stated that "saturation is the truly optimal state of ascorbic acid nutrition for the infant since in the event of an increased demand or decreased supply, the vitamin depot is presumably larger than in partial saturation."[337] The same argument would seem to be valid for the growing child. Since vitamin C is intimately concerned with cellular metabolism, liberality in allowance throughout the entire period of growth seems logical. There is still considerable difference of opinion concerning the satisfactory allowance for the adult. While it may be safe to accept the middle level of requirement, the upper level of luxus consumption is more in keeping with the policy of providing a generous margin of safety in most dietary allowances. In pregnancy and lactation with their increased demands, the margin of safety afforded by the upper level of requirement is most essential, and this may also hold for elderly persons.

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## Council on Pharmacy and Chemistry

### REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. IN ADDITION THE COUNCIL VOTED TO INCLUDE IMMUNE GLOBULIN (HUMAN) IN N. N. R. AND TO ACCEPT CERTAIN SUBMITTED BRANDS. THE MONOGRAPH AND THE DESCRIPTION OF ACCEPTED PRODUCTS APPEARS IN THIS DEPARTMENT OF THIS ISSUE OF THE JOURNAL.

PAUL NICHOLAS LEECH, Secretary.

### THE PRESENT STATUS OF IMMUNE GLOBULIN (HUMAN)

The Council issued a preliminary report on Immune Globulin (Human) and two submitted brands—Placimmunin-Squibb and Immune Globulin (Human)-Lederle. This report appeared in THE JOURNAL for Aug. 17, 1935,[1] along with an editorial summarizing the report.[2] The conclusion of the report, which was based principally on McKhann's work,[3] read as follows:

"After considering the available evidence, the Council decided that although Immune Globulin (Human) appears to be a promising immunizing agent, more evidence of its value is needed before it may be generally used by the medical profession.

"The Council, therefore, postponed consideration of Immune Globulin (Human) and the brands submitted by Squibb (Placimmunin) and Lederle until such further evidence is available, and authorized publication of the foregoing report."

Subsequently the National Drug Company presented its brand of immune globulin (human). Many additional references have appeared in the literature in the two years since the publication of the previous report and it is therefore essential to consider the present literature.

#### VARIOUS ANTITOXINS CONTAINED IN IMMUNE GLOBULIN (HUMAN) AND THEIR RELATIONSHIP TO TESTING ITS POTENCY

Karelitz[4] concluded from a series of experiments that the protein extract composed of globulins derived from the human placenta contained diphtheria and scarlet fever antitoxins, antibodies which neutralize the virus of acute anterior poliomyelitis and protect exposed susceptible children against measles.

Eley[5] noted that placental extracts had been found to prevent or modify measles in nonimmune individuals who had been infected by the virus; that it neutralized diphtheria toxins; that it blanched scarlet fever reactions and neutralized the virus of poliomyelitis. He also noted that McKhann[6] had determined that the substances antagonistic to the viruses of measles and poliomyelitis were present in all his globulin fractions, whereas the antibodies for scarlet fever and diphtheria were found only in the more soluble pseudoglobulins.

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1. Preliminary Report of the Council: Immune Globulin (Human): Placimmunin-Squibb and Immune Globulin (Human)-Lederle, J. A. M. A. **105**: 510 (Aug. 17) 1935.

2. Immune Globulin (Human) and Measles, editorial, J. A. M. A. **105**: 514 (Aug. 17) 1935.

3. McKhann, C. F., and Chu, F. T.: Antibodies in Placental Extracts, J. Infect. Dis. **53**: 268 (March-April) 1933. Schick, Bela, and Karelitz, Samuel: Studies in Prophylaxis of Measles, Am. J. Dis. Child. **47**: 1162 (May) 1934. McKhann, C. F., and Chu, F. T.: Use of Placental Extract in the Prevention and Modification of Measles, Am. J. Dis. Child. **45**: 475 (March) 1933. McKhann, C. F., and Condy, Harriet: Immunity in Infants to Infectious Diseases: Placental Antibodies, South. M. J. **27**: 20 (Jan.) 1934. McKhann: Totals in table 3 (not published elsewhere).

4. Karelitz, Samuel: Measles Prophylaxis, New York State J. Med. **35**: 876 (Sept. 1) 1935.

5. Eley, R. C.: Placental Extract (Immune Globulin Human) with Especial Reference to Its Use in Prevention and Modification of Measles, J. Michigan M. Soc. **35**: 769 (Dec.) 1936.

6. McKhann, C. F.; Green, A. A., and Condy, Harriet: Factors Influencing Effectiveness of Placental Extract in Prevention and Modification of Measles, J. Pediat. **8**: 603 (May) 1935.

Karelitz, Greenwald and Klein[7] noted that the prophylactic value of this substance could not be reliably determined by its nitrogen content and that McKhann's studies had indicated that this substance, which was extracted from the human placenta, contained antibodies for measles and for diphtheria. Karelitz and his associates noted that for all practical purposes the globulin had been shown to be as effective as blood serum used for the same purpose. They concluded that the immunizing value of the amount of maternal blood serum which contains one unit of diphtheria antitoxin should be equivalent to the amount of immune globulin which contains one unit of diphtheria antitoxin. They tested this hypothesis by adjusting the amount of immune globulin used in immunizing their patient on the basis of the diphtheria antitoxin titer. As a result their dosage varied from 37 to 20 cc. in obtaining results similar to those obtained by administering 10 cc. of adult serum. They suggested the application of this method to the evaluation of various lots of immune globulin expressed from the placenta.

Karelitz and Greenwald[8] studied the possible source of the antibodies which these placental extracts contained. They expressed the belief that the immunizing properties of the placental fluid (extracellular constituents of the placenta) was actually comparable to that of the blood serum. They compared the antitoxic titer of maternal circulating blood with the serum extracted from the placenta and concluded from their studies that the activity of the globulin which was obtained from the placental fluid could be tested as accurately against the fluid as against the maternal circulating blood.

### THE IMMUNITY PRODUCED BY MODIFIED MEASLES

In considering a preparation which is proposed primarily for the purpose of modifying a disease, it is well to study the degree and extent of the immunity which results from such modified disease in comparison with the immunity following an unmodified case of the same disease.

Townsend[9] made a special study of this particular question. He instituted a ten year follow-up on a series of thirty-two patients given 9 cc. of convalescent whole blood for the prevention of spread of a measles epidemic in a boarding school. None of the thirty-two developed measles during the subsequent ten year period. Nine of them gave a definite history of exposure and five others a questionable history of exposure (in the presence of an epidemic without any direct known contact). The author concluded that there was no evidence that the immunity conferred by modified measles (in this series with convalescent whole blood—not immune globulin) was any less than that which followed unmodified measles.

McKhann[6] found that the immunity which followed the prevention of measles by the injection of immune globulin was passive in type and of short duration. For that reason he did not believe that the preparation should be used for that purpose except in institutions, for small infants and for those suffering from other illnesses. He noted that it remains to be determined to what degree measles can be modified and still permit the development of a permanent immunity. Ordinarily it is considered that permanent immunity usually follows the modified as well as the unmodified disease. It is granted that it is important to note that the permanence of immunization has not been determined. Nevertheless, the agent appears to be as useful as other immunizing agents employed to modify or prevent the disease.

### IMMUNE GLOBULIN (HUMAN) AND OTHER IMMUNIZING AGENTS

Karelitz,[4] after an extensive review of the literature and study of his own cases, concluded that the therapy of choice in the prevention of measles was convalescent serum; that adult blood and serum were effective and practicable; that placental extract was effective, but that reactions were sometimes severe and that the proper dosage must be accurately determined in order to obtain the desired results. He included in his work table 1. The results noted in this table indicate that there is little difference between the three agents employed, provided they are properly standardized and administered on the basis of the standardization.

Blackler[10] used adult immune serum in the immunization of 105 patients, twelve of whom developed "full-blown" measles (all these twelve patients were given the serum of the same donor). Eight developed modified measles, five of these from the donor referred to and eighty-five were entirely protected by the use of this serum, which was obtained from patients giving a definite history (with the exception of the donor mentioned) of measles.

Eley[5] noted that the effectiveness of immune globulin as it is employed in the immunization of measles depended on the dosage, potency, the type of exposure, the time element, the age and the size of the patient. He further noted that the desirability of protection or modification depended on the circumstances; that modification is desirable in most home cases provided the children were not too young to be exposed to even a mild case of measles; that absolute prevention was essential in the control of measles in hospitals and institutions. He reviewed the literature and concluded that the evidence indicated that it was a valuable preparation in the prevention or modification of measles but that its use as an immunizing factor in other diseases had not yet been established.

### PREVENTION AND MODIFICATION; HOME CASES AND INSTITUTIONAL CASES

As noted by Eley[5] and previously by Karelitz[4] there is considerable difference in the actual administration of this immunologic agent, depending on whether measles is occurring in the private home or in institutions. Karelitz, Greenwald and Klein,[7] after reviewing the work of McKhann and his associates,[6] decided to employ immune globulin (human) in the treatment of intimate home exposures, feeling that this would give a more adequate test and more accurate evaluation of the product than was obtained with McKhann's institutional series. As previously noted, after varying their dosage in accordance with their own standardization (given previously) they obtained results which were comparable to those obtained with 10 cc. of adult serum.

Table 1.—*Results Obtained by Karelitz*

| Authors | Dosage | No. | Protected | Modified | Failed |
|---|---|---|---|---|---|
| Morales and Mandry: Bol. Asoc. med. de Puerto Rico 22:217 (Nov.) 1930 | 10 cc. of adult serum | 138 | 40% | 40% | 20% |
| Karelitz and Schick: J. A. M. A. 104:991 (March 23) 1935 | 10 cc. of adult serum | 70 | 42% | 41% | 17% |
| Karelitz: New York State J. Med. 35:870 (Sept. 1) 1935 | 20 cc. immune globulin calculated to correspond to 10 cc. of adult serum | 74 | 39% | 42% | 19% |

Laning and Horan[11] employed immune globulin in a series of ninety-three cases. No serious case of measles developed, and in the typical cases which occurred complications did not develop. There was a control series of forty-six cases in which there were twenty-six severe cases, in fifteen of which complications occurred and two of which were fatal. These authors did not encounter alarming reactions and believed that the preparation was comparable to convalescent serum. They pointed out that it had the advantage of always being available. These authors administered 2 cc. to seven patients and 10 cc. to twelve patients from one to four days after exposure. The seven patients had light attacks of measles and the disease was prevented in the twelve cases. They then administered 2 cc. in seventy-four cases in which it was difficult to determine the date of exposure and the optimum time for administering a modifying dose. Light cases of measles developed in sixty-eight and moderate cases of measles in the six others. There were no severe cases and no

7. Karelitz, Samuel; Greenwald, C. K., and Klein, A. J.: A Method of Determining Dosage of Placental Globulin in Measles Prophylaxis, Proc. Soc. Exper. Biol. & Med. 32:1359 (May) 1935.

8. Karelitz, Samuel, and Greenwald, C. K.: Comparison of Maternal Circulating Blood Immunity with that of Placental Fluid, Proc. Soc. Exper. Biol. & Med. 32:1362 (May) 1935.

9. Townsend, J. H.: Does Modified Measles Confer Lasting Immunity? New England J. Med. 214:732 (April 9) 1936.

10. Blackler, C. F.: Adult Immune Serum in Measles Control, Canad. Pub. Health J. 27:587 (Dec.) 1936.

11. Laning, G. M., and Horan, T. N.: Immune Globulin Used as Preventive and Modifier of Measles, J. Michigan M. Soc. 34:772 (Dec.) 1935.

complications among those who were given immune globulin. The results are indeed surprising, since the modifying agent was given in this series at various indefinite points between exposure and prodromal symptoms.

Gottlieb[12] published a preliminary report on the use of immune globulin in the prevention of German measles in a hospital. In sixteen cases, all subjects being members of the staff, he injected 4 cc. intramuscularly and in another forty-six similar cases he injected 0.2 cc. intradermally. German measles did not develop in any of these cases, whereas nine cases of German measles developed in the control series of eighteen untreated similar cases. He expressed the hope that his report would stimulate further experimentation in the field and concluded that immune globulin was a useful measure for the prevention of the spread of an epidemic of German measles in an institution.

Goldstein, Eisenoff and Blauner[13] reported on the use of immune globulin in an institutional epidemic of measles. These workers did not attempt to immunize all the patients in the hospital at once but determined first that exposure had taken place in each ward and on each floor before instituting immunization of patients in that section of the hospital. Goldstein and his co-workers immunized forty-nine persons, thirty-two of whom developed measles, five severe and twenty-seven mild, and only five developed complications. None of the persons who developed measles died but it is evident from the authors' results that there was a reduction in the severity of the disease and in the complications resulting from measles.

Salazar de Souza,[14] after referring to his original report[15] on the use of placental blood, noted that the 1934 Lisbon epidemic had given him an additional opportunity to complete his research in this field. He at first had used formaldehyde in the preparation of his serum and blood, but he found that this attenuated the immunizing factors and substituted tyndallizations of from 52 to 54 degrees. He later added merthiolate 1:1,000, one part to three of the finished serum, and found that the immunizing factor was not attenuated. He continued, however, to use a single tyndallization at 54 degrees for one hour. Using from 4 to 5 cc. of the preparation derived in this manner, he obtained immunization in 80 per cent of his cases and using from 6 to 6.5 cc. in another series he obtained immunization in 100 per cent of the cases. He noted the failure reported by Accordini[16] but felt that the results obtained by the latter, while negative, were more or less in accord with the fact that the injections were given from the fifth to the eighth day rather than before the fifth day after exposure.

TABLE 2.—*Results Obtained by McKhann, Green, Eckles and Davies*

| | | Protected | Modified | Failed |
|---|---|---|---|---|
| Given to prevent*..... | 18 | 7 | 5 | 6 |
| Given to modify†..... | 66 | 15 | 32 | 19 |

* Early in incubation period.
† Late in incubation period.

### REACTIONS

In one series of ninety-three cases[11] there were eighteen reactions, eight of which occurred from the administration of 10 cc. doses. Reactions were both local and general but subsided within twenty-four hours. There had been local reactions in 35 per cent, severe local reactions in 4 per cent and febrile reactions in 15 per cent, with temperatures of 101 F. in 2.5 per cent. Karelitz[4] considered the reactions a distinct disadvantage. McKhann[6] studied the immunizing property of globulin fractions with the hope of finding a preparation equally successful but with fewer reactions. In all instances he found that refinement and concentration resulted in lowered potency, although all the preparations had some immunizing activity. Later he used the immune globulin orally in an attempt to avoid measles.

### ORAL ADMINISTRATION

McKhann, Green, Eckles and Davies[17] were able to render twenty-two children negative to the Dick test for periods up to eighteen days by the oral administration of from two to three times the amount of immune globulin (human) that is usually injected for immunization against measles. (Periods lasting eighteen days occurred only if the immunizing substance was served in iced alkaline carbonated water.) The preparation was always administered in cold water on an empty stomach. These results could not be obtained in adults, although the authors believed that the test suggested the effectiveness of the oral administration of this substance in the prevention and modification of measles. This was done in an attempt to avoid reactions seen with the injection of this material. In accordance with their expectations, no reactions occurred in the series of twenty-two patients given the substance orally. Table 2 indicates their study of the oral administration of immune globulin (human) for prevention and modification of measles. It is obvious that the results were not particularly good but also that it at least had the advantage of not producing any reactions.

It is obvious from the results in this small series of cases that the oral administration of this preparation is still in an early experimental stage.

### AVAILABILITY

One of the principal advantages of the use of immune globulin (human) is that it is more available than the other agents which are used for the same purpose. This fact has been pointed out by many of the authors who have promoted and continued the study of its usefulness. Chu and Chou[18] went one step further and prepared a dry form which they found convenient for the purpose of pooling and of storage without deterioration. They tested the product in a series of twenty-two cases by intramuscular injection with the following results: prevention, five cases; very mild measles, seven cases; mild measles, two cases; slightly modified measles, five cases, and unmodified measles, three cases.

### SUMMARY

At the time of the previous consideration by the Council of immune globulin (human) the evidence was considered inadequate on which to give it further consideration. A study of the literature which has become available since that report was published indicates that the following points are of importance:

1. The use of the diphtheria antitoxin titer is entirely satisfactory as an adequate basis for determination of the measles immunizing potency of the preparations.

2. The degree of modification which is accomplished by the various immunizing preparations apparently determines whether or not a temporary or permanent immunity is conferred.

3. The reports seem to be about equally divided on the question of whether or not this immunizing agent is superior to convalescent serum.

4. It is as useful for the modification of measles in home cases as it is for prevention in institutional cases.

5. The reactions are not infrequent and not always mild following the use of this agent, and attempts to avoid them have included refinement and concentration as well as oral administration instead of injection of the immunizing agent.

6. The preparation has a greater availability than the other immunizing agents.

7. The advantages and disadvantages of immune globulin (human) as an immunizing agent in the prevention and modification of measles are at least equal to those of other preparations which have been used for a similar purpose.

12. Gottlieb, Julius: Placental Extract in the Control of German Measles: Preliminary Report, Maine M. J. 27:10 (Jan.) 1936.
13. Goldstein, Hyman; Eisenoff, Henry M., and Blauner, Samuel A.: Use of Immune Globulin in the Prophylaxis of Measles, Am. J. Dis. Child. 55:110 (Jan.) 1937.
14. Salazar de Souza, Jaime: Immunization Against Measles by Placental Blood, Arch. de méd. d. enf. 39:282 (May) 1936.
15. Salazar de Souza, Jaime: Active Aspecific Transitory Immunization Against Measles by Use of Placental Blood, Arch. de méd. d. enf. 35:633 (Nov.) 1932.
16. Accordini, G.: Morbillo ed immunizzazione (Results of Immunization with Placental Blood), Clin. Pediat. 15:572 (July) 1933.
17. McKhann, C. F.; Green, A. A.; Eckles, L. E., and Davies, J. A. V.: Immunologic Applications of Placental Extracts: Effectiveness by Oral Administration, Ann. Int. Med. 9:388 (Oct.) 1935.
18. Chu, F. T., and Chou, C. Y.: Use of Dry Form of Placental Extract in Modification of Measles, Chinese M. J. 50:297 (April) 1936.

## NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

**IMMUNE GLOBULIN (HUMAN).**—A preparation of globulins made from human placental blood and containing immune factor or factors against measles. The immunizing potency of the product is determined on the basis of the diphtheria antitoxin titer of the placental blood.

*Actions and Uses.*—Immune globulin (human) is useful in the prevention and modification of measles. It is equivalent in usefulness to convalescent serum but has the advantage of universal availability. It has the disadvantage of producing reactions not always mild. Most reactions, however, can be avoided by the administration of the proper dosage, which is necessarily modified in accordance with the stage of the incubation period or the prodromal stage of the disease. It is useful in the prevention of measles in institutional cases in larger doses than those given for modification. Prevention is, of course, less desirable than modification except where younger children ill with other diseases are apt to contract measles by exposure to a modified case. Otherwise it is more desirable to permit a child to have mild measles so that immunization occurs rather than to prevent the disease and leave the child nonimmune to subsequent attacks of the disease. Protection should not be attempted until definite exposure has taken place. Immune Globulin (Human) has also been used in the treatment of measles. Attempts to avoid reactions have led to refinement and concentration of the product and even to its oral administration, which cannot be advocated on the basis of the evidence which is available at present.

*Dosage.*—The amount of immune globulin (human) which should be injected in a given case depends on the following factors:

1. Whether modification or prevention is desired.
2. The age and general condition of the patient.
3. The intimacy of exposure, the stage of the disease and the virulence of the infection.

Careful consideration of the available literature is necessary to evaluate properly these factors and determine an entirely satisfactory dosage, and even then it is not always possible to be certain of not obtaining prevention when modification is desired and vice versa. The following doses are recommended merely as a general pattern and are subject to adjustment in accordance with the factors listed above: for prevention, 2 to 5 cc.; for modification, 2 to 10 cc.; for treatment (with caution), 5 to 10 cc.

E. R. Squibb & Sons, New York.

*Immune Globulin (Human)—(Placimmunin).*—Human placentas from healthy mothers are extracted with 2 per cent sodium chloride solution for forty-eight hours at approximately 40 F. The soluble material is decanted, centrifuged and refined in a manner essentially that used in the concentration of antitoxins, ammonium sulfate being used as a precipitant. The final precipitate containing the antibody-bearing globulins is dialyzed to remove sulfates, centrifuged, filtered through a bacteriologic filter, tested for sterility and assayed on guinea pigs for its power to neutralize a measured dose of diphtheria toxin.

Marketed in packages of 2 cc. and 10 cc. vials, each sealed with a rubber diaphragm.

**DIPHTHERIA TOXIN-ANTITOXIN MIXTURE** (See New and Nonofficial Remedies, 1938, p. 406).

The Gilliland Laboratories, Inc., Marietta, Pa.

*Diphtheria Toxin-Antitoxin Mixture, 0.1 L+ (Goat).*—Each cubic centimeter represents 0.1 L+ dose of diphtheria toxin neutralized with the required amount of diphtheria antitoxin obtained from the goat. Marketed in packages of three 1 cc. vials, and in packages of three 1 cc. syringes (one immunizing treatment); in packages of thirty 1 cc. vials (ten immunizing treatments); and in single vial packages containing, respectively, 10 cc., 20 cc., and 30 cc.

**ANTIPNEUMOCOCCIC SERUM, TYPE II** (See New and Nonofficial Remedies, 1938, p. 399).

Parke, Davis & Company, Detroit.

*Antipneumococcic Serum (Felton) Type II, Refined and Concentrated.*—An antiserum containing predominantly antibodies of type II pneumococcus (Diplococcus pneumoniae) prepared by immunizing horses with killed cultures of highly virulent Diplococcus pneumoniae isolated from lobar pneumonia. The product is refined and concentrated by the method of Dr. L. D. Felton (*J. Infect. Dis.* 42:543 [Dec.] 1928) and contains antibacterial properties against type II Diplococcus pneumoniae. The potency of the product is expressed in terms of the unit described by Dr. Felton, one unit being that amount of serum which, when injected simultaneously with a given test dose of culture, will protect for ninety-six hours at least 60 per cent of the test mice. It is also tested by the precipitation test designed by Dr. Felton. The finished product contains some type I pneumococcus antibodies. It is marketed in two packages of one syringe, one containing 10,000 and the other 20,000 Felton units of type II Diplococcus pneumoniae; each package contains also a vial of normal horse serum (1:10 dilution) for reaction test.

**THIAMIN CHLORIDE** (See THE JOURNAL, July 16, 1938, p. 253, and the Supplement to N. N. R., 1938, p. 17).

**Thiamin Chloride-Squibb.**—A brand of thiamin chloride-N. N. R.

Distributed by E. R. Squibb & Sons, New York.
*Ampule Solution Thiamin Chloride-Squibb, 1 cc.*
*Tablets Thiamin Chloride-Squibb, 1 mg.*
*Tablets Thiamin Chloride-Squibb, 5 mg.*

**EPHEDRINE SULFATE** (See New and Nonofficial Remedies, 1938, p. 228).

**Ephedrine Sulfate-Upjohn.**—A brand of ephedrine-sulfate-U. S. P.

*Capsules Ephedrine Sulfate-Upjohn, ½ grain (0.025 Gm.).*
*Capsules Ephedrine Sulfate-Upjohn, ¼ grain (0.05 Gm.).*
*Ampoules Ephedrine Sulfate-Upjohn, ¾ grain (0.05 Gm.).*
Manufactured by The Upjohn Co., Kalamazoo, Mich. No U. S. patent or trade mark.

## COUNCILS' COMMITTEE ON CONTRACEPTIVES

THE FOLLOWING REPORT WAS PREPARED UNDER THE AUSPICES OF THE COUNCILS' COMMITTEE ON CONTRACEPTIVES AND PUBLICATION HAS BEEN AUTHORIZED.

PAUL NICHOLAS LEECH, Secretary,
Council on Pharmacy and Chemistry.

HOWARD A. CARTER, Secretary,
Council on Physical Therapy.

## REPORT ON THE USE OF ROENTGEN RAYS FOR CONTRACEPTION

In 1932 Harris[1] and in 1936 Mayer, Harris and Wimpfheimer[2] published articles dealing with the use of roentgen rays to produce therapeutic abortion. Their results were satisfactory and, in their opinion, superior to surgical procedures in pregnancies of less than fourteen weeks' duration. This method they advocated as particularly desirable in cases in which surgery is hazardous or contraindicated for medical reasons. Following this treatment there is a period of amenorrhea for about two years in women under 35 years of age. In women over 35 the amenorrhea may be permanent.

At the organization meeting of the Councils' Committee on Contraceptives, it was suggested that roentgen rays had been used to cause sterility in women or to interrupt pregnancy for nonmedical reasons. The impression was given that this procedure may be more generally practiced than is believed. Dr. A. U. Desjardins, in an effort to determine how extensively roentgen rays are being used for these purposes, wrote to twelve radiologists throughout the country. In all but one instance the replies from these men stated that they were not aware of such a practice, certainly on the part of reputable members of the profession, and were doubtful whether this technic was being employed to any appreciable extent by less scrupulous practitioners. That this practice has been conducted by a few physicians has apparently come to the attention of a prominent radiologist in an eastern city, but he adds that there has been no legal issue, to his knowledge.

If roentgen rays are being used to induce abortion or to produce sterility it seems highly improbable that it is a very common practice, as it has not come to the attention of radiologists throughout the country. Certainly reputable radiologists are not engaged in this practice and, if men of lesser ethical principles are employing this method, they are doing so very unobtrusively. In spite of the results reported by the workers mentioned in the use of roentgen rays for therapeutic abortion, it is the opinion of radiologists and other members of the medical profession that this method is decidedly dangerous and that its use should be deprecated. It is needless to say that the use of roentgen rays to produce abortion in cases in which emptying of the uterus is not required for therapeutic reasons is contrary to all the ethical principles of medical practice.

1. Harris, William: Am. J. Roentgenol. 27:415 (March) 1932.
2. Mayer, M. D.; Harris, William, and Wimpfheimer, Seymour: Am. J. Obst. & Gynec. 32:945 (Dec.) 1936.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 5, 1938

## ISOLATION FROM HUMAN BEINGS OF EQUINE ENCEPHALOMYELITIS VIRUS

In this issue of THE JOURNAL are two papers (pages 1734 and 1735) reporting in two widely separated areas in the United States cases of human encephalitis, the causal relation of which to epidemic equine encephalomyelitis seems to have been proved. One of the outbreaks apparently was due to the western strain and the other outbreak due to the eastern strain of equine encephalomyelitis.

Isolation of eastern equine encephalomyelitis virus from the brains of children who died from encephalitis and proof that the virus thus isolated is infectious on intranasal instillation into mice are recent notable contributions to epidemiologic knowledge.[1] This is apparently the first horse virus definitely implicated in a human disease.

During August and September an outbreak of the eastern type of equine encephalomyelitis occurred in southeastern Massachusetts, accompanied by several fatal cases of encephalitis among children. Fothergill and his colleagues[2] reported the isolation of the horse virus from the brain of one of these patients. Brain tissues from seven other patients were placed in sterile glycerin by Pope and Feemster of the Massachusetts State Department of Health and sent to Webster and Wright[3] of the Rockefeller Institute for detailed microbic analysis. The New York consultants made a 10 per cent suspension of these tissues in hormone broth and injected 0.03 cc. doses of the resulting supernatant fluid intracerebrally into 3 weeks old Swiss mice. Forty-eight hours later mice injected with four of the seven human brain samples showed ruffled fur and lethargy, alternating with slight convulsive twitchings. The mice soon became prostrate, showed severer and more frequent convulsive movements, and died by the seventy-second hour. Cultures from the brains and organs of these mice were bacteriologically sterile. The brains of certain of these mice were emulsified and injected intracerebrally into second generation mice. Mice thus injected became ill within forty-eight hours and died within seventy-two hours. Third and fourth generation mouse brains were emulsified and filtered through a Seitz pad. Mice injected with the resulting filtrates developed typical symptoms and succumbed by the third day. This successful filtration proved that the infectious agent is a virus of relatively small dimension.

The virus was found to be highly infectious for mice by nasal instillation. Third generation mouse passage virus was fatal to monkeys and guinea pigs when injected intracerebrally in large doses. By the forty-eighth hour the animals appeared dazed, showed muscle weakness and then became prostrate, death usually occurring between the seventy-second and the ninety-sixth hour. Blood and spinal fluid taken at the forty-eighth hour stage were positive for the virus (mouse test). Brains removed just before or soon after death were also infectious. Rabbits were also susceptible to massive intracerebral doses of the virus and usually succumbed within seventy-two hours. Their brain tissues gave positive mouse tests for the infectious agent. Guinea pigs given the virus in the pad usually developed a fatal encephalitis after a latent period of about five days. The relative susceptibilities of the five animal species are characteristic of the eastern horse encephalomyelitis virus. These susceptibilities differ from those of other known viruses which cause infection of the central nervous system in man.

The presumptive identity with the horse virus was confirmed by specific neutralization tests. Of each of the four positive brain emulsions 0.3 cc. was mixed with an equal volume of hyperimmune antiequine-encephalomyelitis rabbit serum (eastern strain). Serial dilutions of the resulting mixtures were injected intracerebrally into mice, with duplicate intraperitoneal injection by the Olitsky technic.[4] The immune serum showed protection effects against from 1,000 to 1,000,000 minimal lethal doses of the brain suspensions. Control tests with normal rabbit serum showed no protection, nor would a specific antiserum against the western strain of horse encephalomyelitis neutralize the infectious agent. This completed the proof of the identity of the human virus with the eastern horse virus.

Now also for the first time neutralization of the western virus of equine encephalitis by human serum has been found.[5] A study of the possibilities of vaccine therapy is now in progress among veterinarians. The conceivable role of field or domestic mice as possible carriers is also under investigation.

1. Wesselhoeft, Conrad; Smith, E. C., and Branch, C. F.: Human Encephalitis, this issue, p. 1735.
2. Fothergill, L. D.; Dingle, J. H.; Farber, Sidney, and Connerley, M. L.: New England J. Med. **219**: 411 (Sept. 22) 1938.
3. Webster, L. T., and Wright, F. H.: Science **88**: 305 (Sept. 30) 1938.
4. Olitsky, P. K., and Harford, C. G.: J. Exper. Med. **68**: 173 (Aug.) 1938.
5. Eklund, C. M., and Blumstein, Alex: The Relation of Human Encephalitis to Encephalitis in Horses, this issue, p. 1734.

## RECENT DEVELOPMENTS IN THE TREATMENT OF UNDULANT FEVER

The increased recognition and incidence of undulant fever has fortunately been associated with new and improved methods of treating this disease, in both its acute and its chronic form. Vaccination has been employed for about ten years, in many instances with apparent success. Huddleson and Johnson [1] have used a liver broth filtrate of the Brucella organism for intramuscular injection. This preparation is known as brucellin; the intramuscular injection of this filtrate has usually resulted in a local reaction and a rise in temperature. If precautions are taken to determine the sensitiveness of the patient before administration, these authors believe that it can be used without dangerous consequences. Foshay and his associates [2] have employed detoxified bacterial antigens in the preparation of an antiserum for the treatment of undulant fever. Goats were used at first in the preparation of this antiserum but more recently horse serum has proved equally satisfactory. Flippin [3] has recently reported encouraging results in the treatment of five cases of undulant fever with a sterile polyvalent antimelitensis serum of bovine origin. Convalescent serum, transfusion with whole blood and vaccines prepared in still other ways [4] have also been reported as sometimes successful in the treatment of this disease. While sufficient evidence has not yet become available to determine which of these methods of therapy is the more effective, they offer, nevertheless, a hopeful and, at least in some instances, an apparently effective means of therapy.

During the past year favorable reports of the treatment of undulant fever with sulfanilamide or its compounds have rapidly accumulated. Among the reports of successful treatment with sulfanilamide or its derivatives are those by Toone and Jenkins,[5] Manson-Bahr,[6] Richardson [7] and Stern and Blake.[8] From the information available it seems likely that sulfanilamide in rather large doses is necessary but that at least in some resistant cases the results are comparable, if not superior, to any other form of treatment of undulant fever thus far proposed.

Finally, successful results have been claimed for other recently described forms of therapy in undulant fever. Among them are treatment by physically induced hyperpyrexia [9] and the intravenous administration of neoarsphenamine.[10] Although a decision as to the value of any method of treatment in undulant fever is difficult because of the alternation of febrile periods and afebrile pauses, the available methods of therapy are such as to allow the disease to be met with a much more powerful therapeutic armamentarium than existed a few years ago.

1. Huddleson, I. F., and Johnson, H. W.: "Brucellin" a Possible Specific for Undulant Fever in Man, Am. J. Trop. Med. **13**: 485 (Sept.) 1933.

2. Wherry, W. B.; O'Neil, A. E., and Foshay, Lee: Brucellosis in Man: Treatment with a New Antiserum, Am. J. Trop. Med. **15**: 415 (July) 1935.

3. Flippin, H. F.: Treatment of Undulant Fever: A Report of Five Cases Treated with a Specific Polyvalent Serum, Ann. Int. Med. **12**: 232 (Aug.) 1938.

4. Carr, J. G.: The Symptoms, Diagnosis and Treatment of Undulant Fever, Illinois M. J. **73**: 521 (June) 1938.

5. Toone, E. C., and Jenkins, A. M.: Undulant Fever (Brucellosis) Treated with Sulfanilamide, South. M. J. **31**: 478 (May) 1938.

6. Manson-Bahr, P.: The Action of Sulfanilamide on Brucella Abortus Infections, Practitioner **140**: 740 (June) 1938.

7. Richardson, L. A.: Infection with Brucella Abortus Treated with Prontosil, Lancet **1**: 495 (Feb. 26) 1938.

8. Stern, R. L., and Blake, K. W.: Undulant Fever: Its Treatment with Sulfanilamide, J. A. M. A. **110**: 1550 (May 7) 1938.

9. Prickman, L. E.; Bennett, R. L., and Krusen, F. H.: Treatment of Brucellosis by Physically Induced Hyperpyrexia, Proc. Staff Meet., Mayo Clin. **13**: 221 (May 25) 1938.

10. Wainwright, C. W.: Melitensis Infection: Treatment with Neoarsphenamine, South. M. J. **30**: 600 (June) 1937.

## PROSTITUTING THE INITIATIVE!

In several states by constitutional amendment the people have the right to vote directly on legislation which they themselves initiate or on measures already passed by the legislature. By this means the laws of the state may be made more clearly to reflect the will of a majority of the voters. The initiative procedure, however beneficial its attributes may be theoretically, has unfortunately been utilized by small groups to foster schemes for selfish ends. On November 8 the people of three states will vote on measures initiated by such groups.

In California a measure initiated by a small group of emotionalists seeks to cripple scientific research in the state by making it difficult if not impossible to procure animals for experimental purposes. In Oklahoma an initiative measure proposes, among other things, to permit hospitals legally to enter into contracts for medical services, if the hospital is organized "on a mutual and cooperative nonprofit plan in connection with some recognized farm or labor union or church or charitable organization." In Colorado, initiative amendment No. 2 proposes by constitutional amendment to guarantee to every person in the state the exclusive right to choose his own state license system of healing and physician for state-required examinations or for therapeutic services in connection with state compensation or other insurance benefits and to open the doors of all tax-supported or partially tax-supported corrective, therapeutic or eleemosynary or other public institutions in the state to the cultists. The Colorado amendment, if adopted, will repeal the basic science act enacted by the legislature in 1937, will deprive the legislature of any future right to exercise its police power in protecting the people from the ministrations of incompetent healers and will devolve on any profession recognized by the state the "exclusive right to examine, license and regulate the practice of its own members through its own legally constituted power or authority."

It seems inconceivable that these measures will receive the approval of the voters in these three states. The tragedy lies in the fact that a procedure conceived in the public interest may be invoked and utilized for purposes inimical to that public interest.

### AMERICAN PUBLIC HEALTH ASSOCIATION MEETING

Elsewhere in this issue (page 1775) appears a brief summary of the discussions relating to medical care at the recent meeting of the American Public Health Association in Kansas City, together with resolutions adopted by the association. Apparently the American Public Health Association failed to place its endorsement on the expressed desire of the president-elect, Dr. Abel Wolman, a doctor of engineering, for the endorsement of the National Health Program in toto as presented by the Technical Committee to the National Health Conference held at Washington in July. Instead it endorsed the proposals of the National Health Conference relating to increased public health services, improvement of hospitalization facilities, care of the medically indigent and compensation for wage losses due to sickness. With respect to the development of health insurance specifically, the association remained silent. It did, however, endorse the statement of the Technical Committee that wide latitude should be given to the development of state plans for carrying out any changes proposed in the delivery of medical service.

The discussion of this issue apparently developed a sharp cleavage in the membership of the American Public Health Association. The lay members of the association, including engineers and sanitarians, were disposed to follow the government's proposals as outlined in the National Health Conference without modification. The medical members of the association, however, including leaders among health officers, executives of volunteer agencies and teachers of public health, were opposed to the endorsement of health insurance proposals made at the National Health Conference. The counsel of the latter group prevailed and the American Public Health Association, therefore, stands officially on virtually the same platform as the American Medical Association. So also does the Conference of State and Provincial Health Authorities of North America. The appointment of a committee of the American Public Health Association to confer with the President's Technical Committee also parallels the action of the American Medical Association.

With the main body of physicians and the main bodies of public health workers committed essentially to the same set of principles and in accord with the government on most of these principles, the best service to the public health may now be rendered by cooperation on those points on which agreement has been reached. Physicians are too important to the public health program and public health workers too important to the physician for either group to permit extremists to drive wedges between them. Efforts to alienate the people from their physicians reflect little credit on the integrity or the judgment of those who indulge in such tactics. The physician stands committed today, as always, to progress in public health, in hospitalization, in medical care for the needy and in defense of the quality of medical care.

## *Current Comment*

### THE COUNCILS' COMMITTEE ON CONTRACEPTIVES

The House of Delegates at its meeting in Atlantic City in 1937 delegated to the Council on Pharmacy and Chemistry and to the Council on Physical Therapy the problem of the investigation of materials, devices and methods recommended or employed for the prevention of conception with a view to determining their physiologic, chemical and biologic properties and effects. The two councils appointed representatives and last spring a Councils' Committee on Contraceptives was organized. The committee is charged simply with studies affecting problems of therapeutic contraception and problems of sterility as well. The first report, which appears on page 1767 in this issue of THE JOURNAL, concerns the misuse of roentgen rays to induce abortion or to produce sterility.

### INTRANASAL MEDICATION

Last year THE JOURNAL [1] called attention to the danger of "lipoid pneumonia" following the intranasal administration of oily preparations. Recently Walsh and Cannon [2] reported that oil, when given in large total amounts and over a long period in this manner to normal rabbits free from upper respiratory infections, seemed to initiate lesions in the lungs which could be demonstrated in roentgenograms. Edema, desquamative alveolitis and focal lipoid pneumonia were produced. As pointed out by these investigators, nasal oils when used clinically or employed because of rhinitis or upper respiratory disease, in passing through infected areas are likely to carry live organisms to the lungs. The combined effect of these factors, therefore, is serious. They instilled medicated oil into a normal rabbit, followed twenty-four hours later by a suspension of live micro-organisms cultured from a rabbit with snuffles; granulomatous lesions were discovered throughout both lungs twenty days after the treatment. These granulomatous lesions contained oil. Intranasal administration of watery solutions of such commonly used medicaments as neosilvol, mild protein silver, tannic acid, zinc sulfate and sodium sulfate, they found, resulted in pulmonary lesions including edema, necrosis and desquamation of macrophages. Such lesions were particularly frequent when antiseptics were given intranasally to rabbits with snuffles or when given mixed with living micro-organisms. The Chicago investigators found that isotonic saline solutions containing such vasoconstrictors as ephedrine and neosynephrin did not cause pulmonary

1. Lipoid Pneumonia and Oil in the Lungs, Current Comment, J. A. M. A. 109:1367 (Oct. 23) 1937.
2. Walsh, T. E., and Cannon, P. R.: The Problem of Intranasal Medication, Ann. Otol., Rhin. & Laryng. 47:579 (Sept.) 1938.

damage after intranasal instillation in normal rabbits. This work, the reports of others, and the additional observations of the same workers [3] point to the potential dangers of intranasal medication and to the tentative conclusion that the only completely safe intranasal medicaments are weak saline solutions of appropriate vasoconstrictors. The use of nose drops containing antiseptics, astringents or oily solutions may be, therefore, of doubtful advisability because of manifest irritating effects on the lungs.

## Association News

### HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

Subsequent to the hearing of the witnesses mentioned in THE JOURNAL last week, the witnesses now include Mr. R. R. Zimmerman, personnel director of the Federal Home Loan Bank Board. Newspapers state that, before Mr. Zimmerman testified, the Grand Jury convened several hours privately with the assistants to the Attorney General who are presenting the government's evidence. Another witness was Mr. William F. Penniman, deputy governor of the Home Loan Bank System and first president of the Group Health Association, Inc. Another witness was Dr. Mario Scandiffio, a member of the staff of the Group Health Association, Inc., and Miss Mary Frances Stuart, laboratory technician of the Group Health Association, Inc. Other witnesses were Dr. Louis R. Marshall of the Veterans Administration Hospital at Batavia, N. Y., and Dr. J. Keith Cromer of Washington, D. C., an obstetrician.

### STATE HEALTH AUTHORITIES SUPPORT AMERICAN MEDICAL ASSOCIATION

The Conference of State and Provincial Health Authorities of North America, in executive session at Kansas City, Mo., October 26, passed the following resolution:

*Resolved*, By the State and Provincial Health Authorities of North America, assembled in special session this twenty-sixth day of October, nineteen thirty-eight, that we hereby express our appreciation and commendation to the House of Delegates of the American Medical Association for their considered action this past September concerning the recommendations laid before our profession at the National Health Conference at Washington, D. C., this past July.

F. J. UNDERWOOD, President.
A. J. CHESLEY, Secretary.

### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).[1]

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The programs to be broadcast in the first group, together with their dates and their topics, are as follows:

Nov. 9. Healthier Boys and Girls.
Nov. 16. Healthful Play.
Nov. 23. Weather and Wearing Apparel.

3. Cannon, P. R., and Walsh, T. E.: Lipoid Pneumonia and Some Potential Dangers of Intranasal Medication, Internat. Clin. 3: 109, 1938.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST; SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

### CALIFORNIA

**Exhibit—The March of Life.**—A sixteen unit display entitled "The March of Life" will make up the exhibit of the University of California Medical School at the Golden Gate International Exposition in 1939. The presentation will show what medicine and surgery have accomplished since the time of Hippocrates and, in addition, demonstrate the services rendered by the university's medical center to its own students.

**Annual San Joaquin Graduate Course.**—The fourth annual graduate study course of the San Joaquin County Medical Society began in Stockton September 22 and will continue each week until November 17. Participating in the course are the following, among others:

Dr. William Dock, San Francisco, Electrocardiography: Its Interpretation and Its Application in Relation to Treatment.
Dr. Hans Lisser, San Francisco, Metabolic Disturbances as Seen in Hyperthyroidism, Myxedema, Calcium Disturbance, Addison's Disease, Cushing's Disease.
Dr. James W. Morgan, San Francisco, Proctology.
Dr. Elliot P. Smart, Murphys, Thoracoplastic Operations.
Dr. William J. Kerr, San Francisco, Clinical Presentation of Medical Cases.

**Symposium on Heart Disease.**—The San Francisco Heart Committee of the San Francisco County Medical Society will hold its ninth annual graduate symposium on heart disease November 15-17. Sessions will be held at the San Francisco, Stanford University and University of California hospitals and Laguna Honda Home. The morning meetings will be devoted to study groups limited to five or ten physicians, covering demonstration of patients presenting problems in heart disease, evaluation of specific diagnostic procedures and therapy, differential diagnosis and treatment. General sessions will be held in the afternoons and evenings; on Tuesday afternoon the diagnosis and treatment of heart irregularities will be discussed; Wednesday, problems in degenerative heart disease, and Thursday, therapy of heart failure. A public meeting will be held Wednesday evening.

### FLORIDA

**District Meeting.**—The Southwest Medical District Society held its second annual meeting at the Dixie Grande Hotel, Bradenton, September 29, under the presidency of Dr. John W. Alsobrook, Plant City. Dr. John F. Mason, Bradenton, president, Manatee County Medical Society, gave the address of welcome. Other speakers, in addition to officers of the state medical society, included:

Dr. Whitman C. McConnell, St. Petersburg, The Insured Neurotic.
Drs. Jere W. Annis and John W. Vaughn, Lakeland, Myocardial Infarction; Electrocardiographic Changes and Necropsy Findings.
Dr. Leldon W. Martin, Sebring, Meckel's Diverticulum.
Dr. Nathan L. Marcus, Tampa, Case of Agranulocytosis with Review of Literature.

### ILLINOIS

**Society News.**—At a meeting of the Tri-County Medical Society in Galesburg October 25 Dr. Warren H. Cole, Chicago, spoke on hyperthyroidism.——The Stephenson County Medical Society was addressed October 27 by Drs. Joseph K. Calvin and Abraham F. Lash, Chicago, on syphilis and puerperal sepsis, respectively.——Dr. Paul H. Harmon, Chicago, addressed the Woodford County Medical Society September 19 on "Diagnosis and Treatment of Suppurative Arthritis of the Hip with Special Reference to Pathologic Dislocation."——The third annual meeting of the Physicians' Association, state department of public welfare, was held in the rooms of the Kankakee County Medical Society, Kankakee, October 12. Dr. Abraham A. Low, assistant state alienist, discussed the newly organized association of former patients of the Psychiatric Institute of the Research and Educational Hospitals, University of Illinois, Chicago, and its implications for the entire group of mental patients, and Dr. Louis Belinson, Elgin, a comparative survey of antisyphilitic treatment in the state hospitals.——The Sangamon County Medical Society was addressed in Springfield October 6, among others, by Drs. Emmet F. Pearson and Darrell H. Trumpe on "Anatomy and Physiology of Chronic Bronchitis and Bronchial Asthma" and "Diagnosis and Management of Minimal Pulmonary Tuberculosis" respectively.

## Chicago

**Dr. de Tarnowsky to Give Armistice Day Lecture.**—Dr. George de Tarnowsky will deliver the Armistice Day lecture sponsored by the faculty and alumni of the University of Illinois College of Medicine Friday morning November 11 in room 423 of the medical school. His paper will be entitled "Twenty Years Later," in which he will review the work done by the medical, dental and nursing corps during the World War. Dr. De Tarnowsky is professor of surgery at the college of medicine.

**Dr. Hektoen to Give Pasteur Lecture.**—Dr. Ludvig Hektoen, executive director of the National Advisory Cancer Council, Washington, D. C., and director of the John McCormick Institute for Infectious Diseases, Chicago, will deliver the fifteenth Pasteur Lecture at a public meeting in the auditorium of the Museum of Science and Industry, Jackson Park, November 22. The lecture will be under the auspices of the Institute of Medicine of Chicago and the Cancer Research Institute of the Chicago Woman's Club. The subject will be "Progress in the Knowledge and Control of Cancer." Through the courtesy of the Museum of Science and Industry, the medical exhibits will be open specially for the meeting. The first Pasteur Lecture was given in 1920 and subsequently each year until 1931. Resumed in 1935, the lectures have been given annually since then. They are designed for laymen.

## INDIANA

**State Medical Election.**—Dr. Karl R. Ruddell, Indianapolis, was chosen president-elect of the Indiana State Medical Association at its annual meeting in Indianapolis October 6 and Dr. Edmund M. Van Buskirk, Fort Wayne, was installed as president. Fort Wayne was designated the place for the meeting in 1939. The association went on record as approving plans for group hospitalization and voluntary sickness indemnity insurance provided they are controlled by physicians.

## IOWA

**Society News.**—The Linn County Medical Society will be addressed November 11 by Dr. Roger Anderson, Seattle, Wash., on "Ambulatory Method of Treating Fractures of the Shaft of the Femur" and "Anatomic Method of Treating Fractures of the Leg." Dr. John P. Peters, New Haven, will discuss nephritis and medical economics before the society December 15.

**Interprofessional Meeting.**—The first annual public health program of the Iowa Interprofessional Association was held in connection with the annual meeting of the Iowa State Association of Registered Nurses in Waterloo October 12 with Dr. Ransom D. Bernard, Clarion, president of the interprofessional association, presiding. The following program was offered:

Harold V. Gaskill, Ph.D., assistant to the dean of industrial science, Iowa State College, Ames, Mutual Interests of the Professions in the Basic Sciences.
Dr. Clifford E. Waller, assistant surgeon general, U. S. Public Health Service, Washington, D. C., A National Health Program—A Review of the Program Recommended by President Roosevelt's Interdepartmental Committee to Coordinate Health and Welfare Activities.
Rev. Maurice Griffin, Cleveland, member, board of directors, American Hospital Association, National Health Conference and the Present Hospitals.

The Iowa Interprofessional Association is supported by the five professional state societies of medicine, dentistry, nursing, pharmacy and veterinary medicine.

## MAINE

**Society News.**—The Kennebec County Medical Association was addressed at its first fall meeting in Waterville September 15 by Drs. John G. Towne on "Tuberculosis of the Bone"; Harvey J. Bourassa, "Ruptured Appendix"; Charles E. Towne, "Stricture of Urethra"; Ovide F. Pomerleau and Moses F. Lubell, "Three Cases of Cancer of the Cervix Treated with Radiation"; Theodore E. Hardy, "Chronic Glomerular Nephritis," and Edwin R. Irgens, "Nasal Plastics."

**Graduate Education.**—A program of graduate education was adopted at a meeting in Bangor October 2 of the editorial board of the *Maine Medical Journal*, the county secretaries, the president and the president-elect of the Maine Medical Association. One method will be the extramural or out of state education in which the physician will study in the larger medical centers through the help of the Commonwealth Fund and the Bingham Associates, while the second will be made available to physicians intramurally or within their own state by the importation of trained teachers who will visit the county medical societies at regular intervals.

## MINNESOTA

**Society News.**—A symposium on sulfanilamide was presented before the Minnesota Pathological Society in Minneapolis October 18 by Drs. Raymond N. Bieter and Wesley W. Spink.——Dr. Justus Ohage Jr. read a paper entitled "Primary Carcinoma of the Pancreas" before the Minnesota Academy of Medicine in St. Paul October 12.——The Scott-Carver Medical Society was addressed at Montgomery October 11 by Drs. George D. Eitel and Ernest L. Meland, both of Minneapolis, on "Traumatic Surgical Emergencies" and "Urologic Emergencies."——The Hennepin County Medical Society, Minneapolis, will be addressed November 7 by Dr. John L. McKelvey on "Gynecologic Malignant Tumors and Their Therapy." Drs. Edward T. Evans and Carl W. Laymon spoke November 2 on "Fractures in Children" and "Skin Disorders in Childhood" respectively.

## MISSISSIPPI

**Gift to Medical School Library.**—The library of the late Dr. John A. K. Birchett, Vicksburg, consisting of more than 500 medical books and about 400 medical journals, was donated to the library of the University of Mississippi School of Medicine recently by his son, Dr. John A. K. Birchett Jr., an alumnus of the school.

**Changes in Health Officers.**—Dr. John W. Duggar, Jackson, associated with the state department of health, has been appointed in charge of the Marshall County health department, succeeding Dr. Vernon B. Harrison, Holly Springs, who has been granted a year's leave of absence to serve as assistant professor of bacteriology and preventive medicine at the University of Mississippi School of Medicine, it is reported.

## NEVADA

**Convention Advocates Health Program Under Existing Agencies.**—The Nevada State Democratic Convention, held in Elko September 27, adopted the following resolution:

We favor a public health program which does not interfere with the personal relations between physician and patient and that is administered through state agencies.

**Committee on Industrial Health.**—The president of the Nevada State Medical Association has appointed the following committee on industrial health: Drs. Ralph A. Bowdle, East Ely, chairman; Robert R. Craig, Tonopah, and Ontie Hovenden, McGill.

## NEW YORK

**Plans for Pneumonia Control.**—Dr. Alexander D. Langmuir, medical consultant of the bureau of pneumonia control of the state department of health, Albany, conducted a series of conferences on pneumonia control in twelve Buffalo hospitals during the week October 10-15 under the auspices of the Medical Society of the County of Erie. Dr. Langmuir also conferred with members of the society who will address lay groups during the winter and gave a talk to nurses at the Buffalo General Hospital.

**Society News.**—Dr. Charles Sidney Burwell, Boston, addressed the Medical Society of the County of Albany, October 26, on "Diagnosis and Treatment of Constrictive Pericarditis."——The Medical Society of the County of Nassau held its second annual members' night September 27; the speakers were Drs. William P. Bartels, Hempstead, on "Surgical Treatment of Acute Subdeltoid Bursitis"; Joseph Millett, Hempstead, "Diabetic Gangrene of the Face," and Carl J. Welge, Roosevelt, "Removal of Foci of Infection in Arthritis."

### New York City

**Legacy to Presbyterian Hospital.**—A cash bequest of $150,000 was left to Presbyterian Hospital in the will of Miss Susan D. Griffith, Saratoga Springs, N. Y., who died September 26. The residuary estate, the value of which was not declared, was also left to the hospital and the institution will receive in addition the principal of several trusts on their termination. The trusts will amount to about $150,000.

**New Superintendent of New York Hospital.**—Dr. George Whiting Wheeler, assistant professor of applied bacteriology, Cornell University Medical College, and clinical bacteriologist at New York Hospital, has been appointed superintendent of the hospital to succeed Dr. Roger R. Hannon, who resigned October 1. Dr. Wheeler has been associated with the college and the hospital since his graduation from Cornell in 1907.

**New Painting of William Beaumont.**—Mr. Dean Cornwell held a private showing at the Waldorf-Astoria October 14 of a painting he recently finished entitled "Beaumont and St. Martin." This is said to be the first attempt by any artist

to reconstruct pictorially the setting and story of Dr. William Beaumont's epoch-making experiments on Alexis St. Martin at Forts Mackinac and Niagara, 1825 to 1835.

**Lay Cornerstone for New College Building.**—The ceremony of laying the cornerstone for a new $1,500,000 building for the New York Medical College and Flower Hospital was held October 20. The date was the fiftieth anniversary of the laying of the cornerstone for the old college building and hospital at York Avenue and Sixty-Fourth Street. The new college will be at One Hundred and Fifth Street and Fifth Avenue. Mayor La Guardia placed the stone, in which were sealed a box from the old cornerstone containing photographs, coins and newspapers of fifty years ago with newspapers of October 20 and other clippings concerning the hospital's history. Besides Mayor La Guardia, speakers included Drs. George W. Crile, Cleveland; John L. Rice, commissioner of health, and Sigismund S. Goldwater, commissioner of hospitals.

**Academy Lectures for the Public.**—The fourth series of lectures to the public presented by the New York Academy of Medicine will begin November 10 with an address by Dr. Cecil K. Drinker, Boston, entitled "Not So Long Ago." The series will include:

Dr. Karl A. Menninger, Topeka, Kan., The Cinderella of Medicine, December 8.
Dr. Walter C. Alvarez, Rochester, Minn., Emergence of Modern Medicine from Ancient Folkways, Jan. 12, 1939.
Dr. Roy Graham Hoskins, Boston, The Story of Mental Diseases, February 9.
Dr. Charles Gordon Heyd, New York, The Romance of Modern Surgery, March 9.
Dr. Sanford V. Larkey, Baltimore, Health in Elizabethan England, April 13.
Dr. Livingston Farrand, Brewster, N. Y., Primitive Man and Medicine, May 11.

## NORTH CAROLINA

**Committee on Industrial Health.**—Dr. Herman F. Easom, Raleigh, has been appointed chairman of a newly created committee on industrial health of the Medical Society of the State of North Carolina. Drs. Marion T. Plyler Jr., Nashville, and Gibbons W. Murphy, Asheville, will serve as members.

## OHIO

**Commissioner of Mental Diseases Appointed.**—Dr. Jesse F. Bateman, superintendent of the Columbus State Hospital, has been appointed commissioner of a newly created division of mental diseases in the state welfare department. An advisory council for the division was also appointed by the governor as follows: Drs. Ora O. Fordyce, Toledo, and Louis J. Karnosh, Cleveland; Judge Dean May, Akron, and Judge Clifford M. Woodside, Youngstown.

## PENNSYLVANIA

**Cancer Meeting.**—A program on cancer was presented at Beaver Falls October 13 under the auspices of the commission on cancer of the Medical Society of the State of Pennsylvania. In the afternoon Drs. Stanley P. Reimann, Philadelphia, and Thomas E. Jones, Cleveland, addressed physicians on "Necessity of Nonspecific Treatment of the Patient" and "Carcinoma of the Colon and Rectum" respectively. In the evening a public meeting was held with Dr. Samuel J. Waterworth, Clearfield, chairman of the cancer commission, and Dr. Reimann as the speakers.

### Philadelphia

**Society News.**—Drs. Paul H. Langner Jr. and Richard A. Kern, among others, addressed the Philadelphia Allergy Society October 26 on "Studies on Local Reactions after Protamine Insulin Injections."——Drs. Josephine B. Neal, New York, and John S. Lockwood addressed the Philadelphia Neurological Society October 28 on "Treatment of Meningitis by Sulfanilamide" and "Sulfanilamide in Experimental Hemolytic Streptococcus Meningitis" respectively.——A joint meeting was held October 28 by the sections on research of the Philadelphia Academy of Stomatology and the Philadelphia County Dental Society; Philadelphia section, International Association for Dental Research and the section on stomatology, Philadelphia County Medical Society. Among the speakers were Drs. Guy M. Nelson, on "Influence of Focal Infection, Especially from the Teeth, on Cholecystitis"; John B. Ludy and Enayat Shirazy, D.D.S., on "Congenital Fistulae of the Lip."

**State Takes Over Byberry Hospital.**—The Philadelphia Hospital for Mental Diseases, commonly known as Byberry, was taken over by the state department of welfare October 22 in accordance with a law passed by a special session of the legislature and signed by Governor Earle September 30. The transfer was delayed when a taxpayer's suit for an injunction was filed and the injunction granted in the Dauphin County Court. The injunction was later dissolved, the court stating that the complainant failed to show that he was seriously damaged by the transfer of the hospital to the state. Dr. Herbert C. Woolley, superintendent of the Pennhurst State School for the Feebleminded, has been appointed superintendent, succeeding Dr. Wilbur P. Rickert. A building program amounting to $7,500,000 has been proposed and now awaits approval for PWA funds to finance it. The transfer of the Philadelphia Hospital for Mental Diseases to the state climaxes a long series of investigations and exposés revealing serious overcrowding in the hospital. The Philadelphia *Record*, in a review of the situation, points out that the newspaper has made periodic investigations and has urged reforms for the past ten years. During the past year there have been investigations by a grand jury, by a committee of physicians and by a legislative investigating committee, finally resulting in legislative action. The hospital is said to have more than 5,600 patients in quarters originally built for 3,500. It will now be known as the Philadelphia State Hospital.

### Pittsburgh

**Society News.**—Drs. Arthur B. Thomas and Leslie H. Osmond addressed the Pittsburgh Academy of Medicine October 11 on "Nature and Treatment of Edema" and "Silicosis and Silicosis with Infection" respectively.

**Hospital News.**—Mercy Hospital celebrated its annual "Mercy Day" September 22 with a clinic and a scientific meeting at which the speaker was Dr. William Boyd, Toronto, Canada, on "Bronchial Carcinoma."——Dr. Evarts A. Graham, St. Louis, gave an address on "Malignant Tumors of the Lung" at the annual observance of "West Penn Day" at the Western Pennsylvania Hospital October 18.

## TEXAS

**Obstetricians and Gynecologists Meeting.**—The Texas Association of Obstetricians and Gynecologists held its annual meeting in San Antonio September 24. Dr. Thomas Benton Sellers, New Orleans, delivered the J. F. Y. Paine address on "Hysterosalpingography—A Valuable Adjunct in Gynecological Diagnosis." Dr. Sellers also spoke at an evening meeting on sterility. Dr. Henry Reid Robinson, Galveston, was chosen president-elect and Dr. Joseph W. Bourland, Dallas, was installed as president. Dr. Roy L. Grogan, Fort Worth, was elected vice president and Dr. Minnie L. Maffett, Dallas, secretary, reelected.

**Society News.**—Drs. Howard O. Smith and Milton A. Davidson, Marlin, addressed the Hill County Medical Society, Hillsboro, September 9 on "Transvaginal Sterilization" and "Obstetrical Analgesia" respectively.——Among the speakers at a meeting of the Palo Pinto-Parker Counties Medical Society, Weatherford, September 6, were Drs. Platt L. Allen, Weatherford, and Joe H. McCracken, Mineral Wells, on "Pertussis" and Roy L. Grogan, Fort Worth, "Dermatologic Problems of the New-Born."——Drs. Rollin S. Fillmore Jr., Jacksboro, and Harold L. Warwick, Fort Worth, addressed the Tarrant County Medical Society, Fort Worth, September 6, on "Varicose Ulcer—Pathogenesis and Rationale of Treatment" and "Otosclerosis" respectively.——Drs. Rufus L. Powers and John Valton Sessums, San Angelo, addressed the Tom Green-Eight County Medical Society September 6 on "Scarlet Fever" and "Carcinoma of the Rectum" respectively.——Dr. James T. Robison Jr., Austin, and W. B. McCall, D.D.S., Temple, addressed the Williamson County Medical Society, Georgetown, September 13 on "Sinusitis in Relation to Cough" and "Focal Infection in the Mouth" respectively.

## WASHINGTON

**Executive Secretary for State Society.**—Mr. Jack M. Geoffroy, Topeka, Kan., recently associated with the research department of the Legislative Council of the State of Kansas, has been appointed executive secretary of the Washington State Medical Association, according to *Northwest Medicine*. Mr. Geoffroy graduated from Washburn College, Topeka, Kan., in 1934 and has been with the Legislative Council since that time.

## WEST VIRGINIA

**Special Society Meetings.**—Dr. George F. Evans, Clarksburg, was reelected president of the West Virginia Tuberculosis and Health Association at the annual meeting in Huntington September 27-28. Among the speakers at the meeting were Drs. Anthony V. Cadden, Hopemont, on "Results of Modern

Methods of Sanatorium Treatment"; Donald L. Butterfield, Charleston, "Medical and Social Problems of Tuberculosis in the Relief Program," and George H. Barksdale, Charleston, "What Parents Should Be Told About Tuberculosis."——The fall meeting of the West Virginia Heart Association was held in Huntington October 13. Guest speakers who conducted clinics and gave addresses were Drs. Samuel Brown, Cincinnati, on "Roentgenologic Diagnosis of Heart Disease"; Julien E. Benjamin, Cincinnati, an electrocardiographic slide demonstration, and Arthur Carlton Ernstene, Cleveland, "Common Errors in Cardiac Diagnosis." At a joint meeting with the Cabell County Medical Society and the West Virginia fellows of the American College of Physicians in the evening Dr. Claude S. Beck, Cleveland, spoke on "Surgery of the Heart."

## WISCONSIN

**Orthopedic Clinics.**—The Sheboygan County Medical Society and the crippled children division of the state department of public instruction sponsored an orthopedic clinic in Sheboygan September 24. Drs. Henry L. Greene, Madison, and Ralph M. Carter, Green Bay, examined the children; members of the staff of the Sheboygan Orthopedic School and the crippled children division assisted in taking histories and interviewing parents. The Eau Claire-Dunn-Pepin County Medical Society sponsored a similar clinic October 12.

**Option on Surgeons' Quarters at Old Fort.**—Efforts are being made by the Wisconsin Daughters of the American Revolution to restore an old building used as surgeons' quarters at Old Fort Winnebago near Portage. The fort was built in 1828 and evacuated twenty years later. For several years the buildings were under the care of a watchman but they were finally sold. Now all the buildings have vanished except the surgeons' quarters, which is "the birthplace of medicine in central Wisconsin," according to the *Wisconsin Medical Journal*. The Wisconsin organization is seeking funds to purchase and restore the building, on which it has an option.

**Society Awards to Drs. Carey and Middleton.**—The State Medical Society of Wisconsin at its annual meeting in Milwaukee in September presented the Council Award, a gold seal of the society, to Drs. Eben J. Carey, dean, Marquette University School of Medicine, Milwaukee, and William Shainline Middleton, dean, University of Wisconsin Medical School, Madison. Dr. Carey was honored for his "high accomplishments in medical education and research" and for his "perfection of the art and dynamic use of visual education as a means of furthering the health of our citizenry." The seal was awarded to Dr. Middleton, according to his citation: "for accomplishments and lofty inspiration in the teaching of students and practitioners, for your quarter of a century of public service and for your outstanding influence in the development of a high quality of medical service for the citizenry of Wisconsin." The gold seal has previously been awarded to twelve physicians.

## GENERAL

**Meeting of Military Surgeons.**—The forty-sixth annual meeting of the Association of Military Surgeons was held at Rochester, Minn., October 13-15 under the auspices of the Mayo Clinic and Foundation. The speakers included:

Capt. George W. Calver, U. S. Navy, Washington, D. C., Is America Physically Fit for War?
Brig. Gen. Leigh Fairbank, D. C., U. S. Army, Washington, Dental Aspects of Preventive Medicine.
Ralph Creer, senior clinical photographer, research department, Veterans' Administration, Hines, Ill., Clinical Photography in the U. S. Army.
Lieut. Comdr. Charles H. Watkins, U. S. N. R., Rochester, Minn., Recent Advances in the Field of Blood Dyscrasias.
Dr. John S. Lundy and Lieut. Lloyd H. Mousel, medical reserve, U. S. Army, Rochester, Present Status of Anesthesia and Its Practical Application in the Combat Zone.
Lieut. J. Grafton Love, Rochester, Low Back and Sciatic Pain Due to Protruded Intervertebral Disks.

The program at the banquet Friday evening was in honor of Rear Admiral Perceval S. Rossiter, surgeon general of the U. S. Navy, who will reach the retirement age November 30. Col. George E. Ijams, Veterans Administration, Washington, discussed "America's Problem." Dr. Thomas Parran, surgeon general of the U. S. Public Health Service, Washington, D. C., was elected president; Major Gen. Charles R. Reynolds, surgeon general of the U. S. Army, Washington, and Drs. Harold D. Corbusier, Plainfield, N. J., James A. Mattison, Los Angeles, and William L. Mann, San Diego, Calif., were elected vice presidents. The 1939 meeting will be in Washington.

**Society News.**—Dr. Everett Morris, Auberry, Calif., was elected president of the American Academy of Tuberculosis Physicians at the annual meeting in San Francisco recently. Drs. Benjamin P. Potter, Secaucus, N. J., and John B. Crouch, Colorado Springs, were elected vice presidents and Dr. Arnold Minnig, Denver, secretary.——Dr. Fred G. Carter, Cincinnati, was chosen president-elect of the American Hospital Association at its recent annual meeting in Dallas, Texas, and Dr. George Harvey Agnew, Toronto, Canada, was installed as president. The 1939 meeting will be in Toronto.——Dr. Hyman I. Spector, St. Louis, was elected president of the Mississippi Valley Conference on Tuberculosis at its annual meeting in St. Louis September 23; W. P. Shahan, Springfield, Ill., executive secretary of the Illinois Tuberculosis Society, was chosen vice president, and A. W. Jones, St. Louis, secretary-manager of the St. Louis Tuberculosis and Health Society, was reelected secretary-treasurer.——Dr. George P. Muller, Philadelphia, was chosen president-elect of the American College of Surgeons at the annual session in New York October 17-21. Drs. Henry W. Cave, New York, and David E. Robertson, Toronto, were elected vice presidents.

**American Congress of Obstetrics and Gynecology.**—Plans are in the making for the first American Congress on Obstetrics and Gynecology to be held in Cleveland Sept. 11-15, 1939. The scope of this congress has been extended beyond that of similar assemblies in the past and will include not only medical groups but those devoted to nursing, public health and institutional administration. National sectional and local societies have approved the congress and have contributed to its support. It is now desired, the announcement says, to obtain a wider representation through the medium of contributing memberships at $5 each. Application for these memberships may be made at the office of the congress, 650 Rush Street, Chicago. In addition to scientific sessions it is planned to provide several evening meetings at which speakers of prominence will address the public. There will also be a comprehensive exhibit, scientific, educational, technical and commercial. The American Committee on Maternal Welfare, which includes in its membership twenty organizations interested in the subject, has been delegated to sponsor the congress. The members of the executive committee in charge of arrangements are Dr. Fred L. Adair, Chicago, general chairman; Dr. Robert D. Mussey, vice chairman, Rochester, Minn.; Miss Sara B. Place, Chicago, secretary; Dr. Rudolph W. Holmes, Chicago, treasurer, and Dr. Frederick H. Falls, Chicago, assistant treasurer.

**Southern Medical Association.**—The thirty-second annual meeting of the Southern Medical Association will be held in Oklahoma City November 15-18 under the presidency of Dr. James W. Jervey, Greenville, S. C. Tuesday November 15 will be Oklahoma City Day, when general clinical sessions will be held on medicine, surgery, gynecology and obstetrics. Tuesday evening there will be a general public session with the following speakers:

Dr. Irvin Abell, Louisville, Ky., President of the American Medical Association, The Role of Surgery in Fighting Disease.
Dr. Thomas P. Sprunt, Baltimore, Diet Fads, Foods and Vitamins.
Rev. Alphonse M. Schwitalla, St. Louis, Society's Debt to the Doctor.

At a general session Wednesday evening Dr. Jervey will deliver his presidential address, entitled "Ars Medica and Ars Poetica." Among speakers who will address the numerous section meetings will be:

Dr. Russell L. Haden, Cleveland, Treatment of Rheumatoid Arthritis.
Dr. Henry F. Helmholz, Rochester, Minn., The Role of Stasis and Infection in Renal Insufficiency of Later Life.
Dr. Jacob Arnold Bargen, Rochester, Minn., Causes of Colonic Cancer: Clinical Support of Current Hypotheses.
Dr. William C. Menninger, Topeka, Kan., Psychoanalytic Principles in Psychiatric Hospital Therapy.
Dr. Robert D. Schrock, Omaha, Bone Tumors.
Dr. Charles O. McCormick, Indianapolis, Analgesia in Labor: Modified Gwathmey Technic.
Dr. Dudley A. Smith, San Francisco, Management of Complex Fistula-in-Ano.
Dr. Edward C. Holmblad, Chicago, Improved X-Ray Technic in Studying Knee Joints.
Dr. Bernard Samuels, New York, Pathology of Complicated Cataracts.

Other groups that will meet during the week are the southern branch of the American Public Health Association, National Malaria Committee, American Society of Tropical Medicine, Southern Association of Anesthetists and region 2 of the American Academy of Pediatrics.

**Warning—Fraudulent Magazine Solicitors.**—The Professional Sales Corporation, New York, reports that one John Bowles, formerly employed by the corporation, is still taking unauthorized subscriptions for various magazines, using both his own name and the alias of John Hamilton. His activities have recently been reported from physicians in Montgomery County, Ohio. The corporation wishes to warn physicians to beware of this impostor and is making every effort to apprehend him. A warning was published in THE JOURNAL July 9.

—The National Publishers Association, New York, reports the fraudulent activities of an agent using the name H. E. Stanton. It is said that this man has operated throughout the country and has victimized physicians exclusively. At one time he was employed by Preferred Publications, Inc., a reliable agency in New York, and absconded with a supply of its order forms. He solicits subscriptions to any and all magazines, many of which the agency does not represent, pockets the full amount of his collections and makes no report of orders to the agency. On some of these orders he has promised a $10,000 accident and travel policy as a premium. He has been in the Southern states, worked his way up the states on the Mississippi River, then eastward and was last heard of in Boston. Physicians are warned to look for this man and avoid any dealings with him. His description is as follows: aged about 38; 5 feet 8 inches tall; weighs about 135; has gray eyes, dark brown hair and fair complexion.

**American Public Health Association Meeting.** — The American Public Health Association at its sixty-eighth annual meeting in Kansas City, Mo., October 25-29, dealt, in addition to its usual scientific program, with the subject of expanded facilities for public health and proposed plans for medical care as outlined in the proposals of the Technical Committee, as presented to the National Health Conference held in Washington in July. The principal speakers were Dr. Thomas Parran Jr., surgeon general of the United States Public Health Service, Washington, D. C.; Abel Wolman, Dr.Eng., president-elect, Baltimore; Arthur J. Altmeyer, chairman of the Social Security Board, Washington, D. C.; Dr. Irvin Abell, President of the American Medical Association, Louisville, Ky., and Prof. Charles E.-A. Winslow of Yale University, New Haven, Conn. Dr. Parran supported the proposals of the National Health Conference and expressed his appreciation of the support given to these proposals, with certain exceptions, by the House of Delegates of the American Medical Association. Dr. Wolman in a somewhat satirical vein intimated that the United States is a century in arrears in public health development, grudgingly conceded that the American Medical Association supported the proposals of the National Health Conference in the main, and intimated that the support was reluctant and tardy. Mr. Altmeyer made a straightforward presentation of the aims of the National Health Conference and outlined the methods by which it was proposed to arrive at the objectives. He emphasized that progress was to be made through state plans and developments with the federal government cooperating principally through furnishing financial grants in aid and technical services. Dr. Abell described the experimentation already carried out by the medical profession in the field of medical care and hospitalization, as well as its traditional support of public health measures. He then set forth the actions of the House of Delegates of the American Medical Association at the special session, September 16 and 17, reading the committee reports verbatim and almost without comment. Professor Winslow, ostensibly speaking for the consumer of medical services, reiterated the familiar arguments about lack of medical care for certain groups in the United States, ridiculed statistical studies other than those in support of his thesis, and attacked the organization and policies of the American Medical Association. In substance he declared that the American Medical Association would never function effectively on the basis of its present organization and should be reorganized on what he termed "a service basis," namely with the hospital as the functional unit of organization instead of the county medical society. He praised the "independent" Committee of Physicians.

The following resolutions were passed by the association:

The American Public Health Association, ever increasingly conscious of the leadership and competence which have characterized the work of the various Federal health agencies, records its unanimous satisfaction in the further evidence of the effective interest of the Federal government in the health of the Nation, embodied in the recommendations of its Interdepartmental Committee to Coordinate Health and Welfare Activities to the National Health Conference, July 18-20, 1938.

There can be no doubt that large areas of many of our States do not enjoy the benefits of adequate health service. We maintain that without adequate local health organization covering every area of the United States, the delivery of the full benefits of modern public health procedure to all the people in the United States cannot be accomplished. We recognize further the indispensable services which State departments of health are capable of contributing over and above those provided under local governmental units in urban or rural communities.

In recognition of these facts, we endorse the recommendations presented before the National Health Conference by the Technical Committee on Medical Care, which propose the expansion of public health services, including necessary medical, hospital and nursing care for the period of maternity and childhood in families unable to obtain adequate care through their own resources.

An appraisal of national health resources reveals the existence of many communities in which hospital facilities are meager or lacking. The inadequacy of institutional facilities presents a handicap to the control of tuberculosis and mental disease, and deprives those requiring care in general hospitals of the full benefits of modern medical treatment. In certain communities adequately supplied with hospitals, economic barriers prevent their full utilization. For large numbers of our population, inadequate income results in inadequate medical and dental care. The concept of the close interrelation of preventive and curative medicine is basic to the modern public health program.

We therefore endorse the recommendations of the Technical Committee to the National Health Conference providing for Federal aid to the States for the construction of additional hospital facilities, the provision of essential medical and nursing care, and hospital care as required, to persons unable to support such care from their own resources, and the compensation against wage loss incurred through sickness. In connection with the Technical Committee's recommendation concerning medical care, the Association supports the view that in the initiation and development of the program, wide latitude should be given to the States in the definition of the population to be served and the method of providing medical service.

We pledge the American Public Health Association to use all its professional resources, and such influence as it has earned through sixty-eight years of development and leadership in Public Health to aid governmental agencies in accomplishing these statesmenlike health objectives.

Furthermore, we offer our cooperation to the governmental agencies which may be charged with the proposed expansion of health services in the United States, and we stand ready to collaborate with other professional and scientific organizations having similar principles and objectives, to the end that at the earliest possible date in every area under the jurisdiction of the United States the whole population may have the benefit of the best that public health service can bring them.

*Be it Resolved*, That the foregoing declaration expresses the formal and considered opinion of the American Public Health Association and that it shall be published in the *Journal*. Be it further

*Resolved*, That the Executive Board is hereby instructed to appoint a representative committee of seven Fellows of the Association to cooperate during the coming year with the Interdepartmental Committee of the United States Government, with the American Medical Association, the American Dental Association, National Organization for Public Health Nursing, the Conference of State and Territorial Health Officers, and with other agencies, to the end that these principles may be translated into effective action.

The most significant difference between the expressions of speakers on the association program and the resolutions as adopted will be found in the silence of the resolutions relating to the question of medical care beyond the statement that "in the Technical Committee's recommendation concerning medical care the association supports the view that in the initiation and development of the program wide latitude should be given to states in the definition of the population to be served and the method of providing medical service."

The following additional resolution was passed:

The American Public Health Association records its appreciation of the participation in its deliberations during this Annual Meeting week of Dr. Irvin Abell, President of the American Medical Association. It records with pleasure its agreement with the approval in principle, at a recent special session of the House of Delegates of the American Medical Association, of the content of the national Health program presented by the Interdepartmental Committee to the National Health Conference. The Association pledges its continued cooperation and support to the American Medical Association in the translation of this policy into action.

Press comment on the meeting was a little confusing. The Kansas City *Times*, October 28, carried a front page story under the headline "For Health Plan: Program Including Compulsory Insurance Endorsed by Public Health Association: Calls for 850 Million: Rift with American Medical Group Which Had Declined to Back Proposal." The story under these headlines declared "In giving approval to the health insurance plan, the association moved further away from the traditional leadership of the American Medical Association." In the Kansas City *Star* of the same date a statement appeared by Dr. Arthur T. McCormack, president of the American Public Health Association, in which he called attention to the fact that the association "by leaving reference to it out of the resolution did not grant approval to the compulsory medical insurance plan of the National program." The Kansas City *Journal* carried a story headlined "Health Experts Silent on Forced Insurance Plan But Follow Lead of A. M. A. on Four Other Planks."

## CORRECTION

**The Nature of the Bleeding in Jaundice.**—In the article by Dr. Armand J. Quick of Milwaukee in THE JOURNAL, May 14, the directions for the preparation of the calcium chloride solution in the section on the quantitative determination of prothrombin (page 1659) should read as follows: Dissolve 1.10 Gm. of anhydrous chemically pure calcium chloride in 400 cc. of distilled water.

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

Oct. 15, 1938.

### Chronic Pneumonia

While chronic pneumonia is well known as a pathologic process, the textbooks do not recognize it clinically. At the Royal Society of Medicine, Dr. J. G. Scadding pointed out that in the nineteenth century great clinical interest was displayed in chronic pneumonia. Laënnec in 1826 described chronic pneumonia following acute pneumonia. Later writers disputed whether chronic indurative pneumonia began with an acute phase. In 1936 Scadding described three cases as "chronic diffuse bronchopneumonia," which ran a chronic course of two years, seven months and three and one half years, respectively, to a fatal termination and simulated pulmonary tuberculosis both clinically and radiologically. At necropsy the essential lesion was a pneumonia in widespread foci showing an unusual variety of modes of progress and spread. Scadding's paper was based on eight cases seen at the Hospital of the British Postgraduate Medical School.

#### CHRONIC CIRCUMSCRIBED NONSUPPURATIVE PNEUMONIA

The usual type of delayed resolution of acute pneumonia falls in this group. While resolution of lobar pneumonia is usually complete in two or three weeks from defervescence, radiologic studies show that complete clearing of opacities may be much delayed—for as long as eighty-five days in one case. Since complete clearing without gross fibrosis is possible, no organization and little suppuration must take place. A similar condition of subacute or chronic consolidation, capable of complete resolution, can arise insidiously or with only mild symptoms at the onset. When it persists for a long time a confusing clinical picture is presented, as in the following case:

A clerk, aged 56, was admitted with a history of increasing weakness and lassitude for eighteen months, loss of more than a stone (6.35 Kg.) and more acute symptoms for seven days, starting with aching in the limbs and one attack of vomiting and cough, mainly unproductive. On admission he was afebrile and he remained so. He looked pale and ill. There was dyspnea on slight exertion. There was diminished movement of the right side of the chest with dulness posteriorly, and weak breath sounds, bronchial in character, in the interscapular region. The scanty sputum was negative for tubercle bacilli; a very mixed flora was found, including coarse spirochetes and fusiform bacilli. X-ray examination showed restriction of movement of the right diaphragm and slight displacement of the mediastinum to the right. Extending out from the right hilar region was an irregular shadow, mainly posterior. Bronchoscopy revealed a normal bronchial tree. A pulmonary growth was suspected. Eight weeks later he was much improved, but the pulmonary signs remained of the same type but were diminished. Three months still later there was complete clearing, and eventually he completely recovered. Chronic suppurative pneumonia may take place with or without abscess formation.

### London's Preparations for Air Raid Casualties

In previous letters some of the extensive preparations made in London for dealing with air raid casualties have been described. The elaborate scheme prepared by University College Hospital for dealing, if necessary, with 1,000 casualties from one air raid was outlined. Further particulars can now be given for the rapid conversion of this hospital into a casualty clearing station. It was arranged to evacuate all the patients. Those who could not be taken to their homes were to be transported to Oxford. The hospital could thus have been emptied in a few hours. Detailed preparations were made for the reception and disposal of casualties. Even the administration of morphine in the darkness, in the event of the lights failing, had not been overlooked and syringes were prepared containing the appropriate doses. For dealing with the gas wounded alone there were twenty-one teams, each consisting of surgeon, assistant surgeon, two dressers and a nurse, working in four shifts. From forty to sixty gas cases could have been treated at one time. Arrangements were made for 100 blood transfusions a day, and there was a cold room for the storage of blood. The outstanding deliveries of medical supplies were called up, giving a three months' supply. The protection of the staff was arranged for in tunnels and basements and gas-proofed rooms, giving accommodation for 380. Places which had not been touched for years were cleared out by the students, giving bomb-proof shelters for 2,000 people.

This is an example of what was done at the great hospitals attached to London's medical schools. The municipal hospitals, which form the largest organization in the world and normally contain 36,000 beds, could coordinate their preparations, as they are all under the control of one authority, the London County Council. Their accommodation was increased by 20 per cent and they were supplied with additional drugs and dressings, estimated to meet the requirements for one month of an acute emergency period. A supply of antitetanus serum was received from the government. Ten of the fever hospitals were supplied by the Ministry of Health with surgical equipment for 5,000 beds. An additional 20,000 blankets were procured. Curtain material and fittings and neon lights were supplied to all hospitals for the purpose of "blacking out." A number of respirators, sufficient for all the patients and staff, candles and torchlights, sand, buckets and shovels to deal with fires from incendiary bombs, sandbags for the protection of vulnerable places, bleach powder for dealing with mustard gas, building materials for the protection of operating rooms, splints and dressings to meet a period of a three weeks emergency were supplied. The Ministry of Health sent 2,000 stretchers to those hospitals. Twenty-one ambulance trains, each with one doctor and seven nurses, were organized. Arrangements were made by which the hospital staffs would all be supplemented at a few hours notice by the allocation of all the school medical and nursing staff available. All the members of the clerical staff of the public health department who were not regarded as essential were allocated to the hospitals for any duties which the medical superintendents could provide. Arrangements were made by which seventy skilled surgeons and assistants would be available for staffing those fever hospitals which were to be upgraded into general hospitals. The result of all this would have been that on October 1 more than 16,000 beds would have been available in the municipal hospitals for the admission of the wounded.

Other preparations made by the London County Council included the addition of 420 units to the London fire department and volunteers to man the auxiliary service, earmarking of commercial vehicles for towing the trailer pumps, augmentation of the normal water supplies and keeping all potential supplies (swimming baths, ponds and the like) full of water. For the augmentation of the ambulance service some 2,000 vehicles and 5,000 women drivers were required. The ministry secured the vehicles, and the need for drivers was being advertised during the crisis.

## PARIS

*(From Our Regular Correspondent)*

Oct. 6, 1938.

### A Symposium on Bone Grafts

The second question to be discussed at the recent International Surgical Congress was "Bone Grafts," the first paper being read by Professor Cuneo of Paris. Opinion was unanimous that the best results followed the use of autoplastic grafts but that success depended on the condition of the bone in which the graft was to be placed. This signified that the bone in which the graft is inserted must possess sufficient regenerative power to form new bone, the graft acting only as a stimulant. Homoplastic and heteroplastic bone grafts are far inferior to the autoplastic variety. Success depends to a great extent on the age of the patient. In children and adults below 50 and in good general condition the chances of a successful outcome are excellent.

Dr. Albert of Liége, Belgium, spoke on the biology of bone grafts, emphasizing that the bone graft per se disappears either partly or completely and is replaced by newly formed bone. In following the laws of osteogenesis in general, the bone graft is an essentially vital phenomenon in which the cells hereditarily destined to form bone play the most important part. The conditions to be fulfilled to have a successful result are to prepare the bed in which the graft is to be placed in such a manner that the tissues forming the bed can give rise to osteogenic buds rapidly; to conserve the periosteal, cortical and medullary portions of the bone constituting the bed; to remove the graft with periosteum intact by mechanical means which do not destroy the vitality of the graft; to prepare the bed before attempting to remove the graft and finally to attempt to stimulate the cellular elements composing the bed by using perhaps in the future the two-step method suggested by Brooks. If these conditions are complied with, the living bone graft is the method of choice. The best chances of survival of the graft are to be expected if thin osteoperiosteal grafts are used as proposed by Ollier and Delagénière when smaller defects need to be filled and the Albee type of graft for larger ones. The latter method will yield more rapid results if early movement is desired.

Dead bone (as suggested by Orell) which has been previously subjected to physicochemical procedures and does not contain any osteogenic element only plays the part of a foreign body which is absorbable and simply acts as a splint until new bone formation has taken place. As all osteogenesis must originate in the osseous tissue around the bed in which any graft is placed, such specially prepared dead bone, termed "os purum," cannot be used when a large graft is called for. Such an objection also holds true for the other type of bone graft, the so-termed os novum, as suggested by Orell. This "os novum" is obtained by inserting a particle of the "os purum" beneath the periosteum of the tibia, representing in reality a living graft. Whether one uses a living bone graft or one in the form of the "os novum" of Orell, success depends entirely on the osteogenic cells, no matter whether they have their origin in the graft itself or in the bed in which it is placed.

Professor Demel of Vienna read a paper on the results of bone grafts in recent bone injuries and pseudarthroses. In recent fractures, especially those due to gunshot or similar modes of injury, bone grafting is rarely indicated. In certain comminuted fractures when good reduction of fragments is impossible or there is a likelihood of the occurrence of a secondary pseudarthrosis, bone grafting is indicated provided one is sure that the bed is not infected. In pseudarthroses when there is a considerable loss of bone tissue the preferable method of treatment is to remove all cicatricial tissue after curetting the medulla of the two bones forming the pseudarthrosis and then transplant some free bone fragments containing both periosteum and compact bone. The use, in addition, of some type of external bone splint is indispensable to assure good fixation of the grafts.

Mr. Platt of Manchester, England, said that he prefers some type of metallic bone splint in fractures to bone grafts. Pseudarthroses should not be operated on too early. Quite frequently simply curetting the ends of the bone and inserting a few osteoperiosteal bone fragments would suffice. If this method did not succeed he preferred a graft taken from the tibia at least for pseudarthroses in the long bones. He had found the shafts of the femur and the lower third of the tibia and of the humerus very unfavorable for bone grafting.

The next speaker was Dr. Svante Orell of Stockholm, who read a paper on the use of the bone graft in tuberculosis of the bones and joints. The "os purum" and "os novum" types of grafts, which he was the first to advocate, had many advantages over the living bone transplant. These newer types of grafts appeared to stimulate not only new bone formation but also the adjacent soft tissues. The "os purum" graft is dead bone which has been deprived of its fats, albuminoids and fibrous tissue by physiochemical procedures. The "os novum" is veritable new-formed living bone obtained by subperiosteal implantation of the os purum. He cited, illustrated by slides, a large number of cases in which these new types of bone grafts had been used in arthrodeses and in tuberculosis of the hip and spine.

The next paper was read by Dr. D. B. Phemister of Chicago on bone grafts in osseous dystrophies and tumors. He cited five personal observations, four of medullary sarcoma and one of cortical sarcoma, which had been treated by resection and bone graft. In two cases involving the upper end of the humerus, one had shown no evidence of recurrence since operation, two and a half years ago; the other had a fracture of the graft and recurrence fourteen months after operation. One case of sarcoma of the ulna had been apparently cured for four and a half years; death occurred in the other of metastases after two and a half years. In the fifth case, a sarcoma of the upper end of the femur, necessitating disarticulation at the hip and insertion of a bone graft from the tibia to give support for an artificial limb, operation was performed five months ago. Benign tumors and bone cysts are favorable cases for operation followed by use of a bone graft, unless there has been a large loss of bone. Two cases, one of the humerus, the other of the radius, of giant cell sarcomas were reported without recurrence for eighteen and twenty-five years respectively. In two cases of bone cyst of the femur no recurrence can be found following removal, thirteen and eight months respectively after operation.

Professor Kappis of Würzburg, Germany, reported a large number of cases in which bone grafts had been employed for chronic (nontuberculous and nonmalignant) arthropathies. He had successful results in 90 per cent of about 500 cases, such as grafts to immobilize the sacro-iliac joint, coxofemoral arthrodesis and fracture of the neck of the femur.

In the discussion of this series of papers, Dr. Danis of Brussels stated that the "os purum" graft of Orell is not as well tolerated as is a metal splint and is expelled after a relatively short interval. It does not possess any osteogenic property but nevertheless it is so easily employed that he has made use of it in many recent complicated fractures as well as in pseudarthrodeses.

Professor Lambotte of Antwerp, Belgium, prefers a metallic splint for pseudarthroses of the humerus and femur, limiting use of the bone-graft to pseudarthroses of the bones of the leg, forearm and clavicle. He believed that a bone graft inserted into the medulla of the ends of the bones does more harm than good, because in case infection supervenes it will be necessary to resect a considerable length of the end of the bones.

Dr. Clery of Chambéry, France, had employed dead bone in forty-eight cases of chronic painful arthritis of the hip with highly satisfactory end results.

Dr. Hybbinette of Stockholm reported six cases of resection of the lower jaw for tumor in which he had filled the defect with a graft taken from the crest of the ilium, a case which is especially adapted for such a graft.

Dr. André Richard of Paris and Berck-Plage, France, prefers living bone grafts and has never used metallic splints in 800 cases of tuberculosis of the spine and in 500 cases of tuberculosis of the hip.

## BERLIN

*(From Our Regular Correspondent)*

Sept. 26, 1938.

### The Fate of Austrian Scientists

A previous letter (THE JOURNAL, June 11, p. 2020) contained an account of the German government's new far-reaching legislation for the erstwhile Austrian state. In the meantime more details of the consolidation of the country since its annexation have been forthcoming and it is possible to report on the fate of many distinguished scientists under the new régime. Through the political upheaval the world famous Faculty of Medicine of Vienna University has suffered severe losses. It is estimated that about half of the assistant professors and instructors holding office at the time the Austrian republic was absorbed by the German reich have lost their positions. The Jewish element has been prominent among these groups whereas but few Jews have served as full professors (ordinarien) in recent years.

The following items concern some of the better known faculty members: Prof. Egon Ranzi, ordinarius in surgery and son-in-law of the Viennese surgeon Anton Eiselsberg, has been forced to relinquish the directorship of the university's surgical clinic and has been retired on a pension because he had been an adherent of Schuschnigg. Profs. Leopold Arzt and Wilhelm Kerl, both of them "Aryans" and ranking dermatologists, met the same fate as Ranzi for like reasons. Professor Arzt, decided anti-Semite, ardent proclerical and nephew of a late archbishop of Vienna, was in custody for a short time. Ernst P. Pick, professor of pharmacology and a pupil and successor of H. H. Meyer, was forced to retire on account of being a Jew. The physiologist Arnold Durig was also retired for reasons unknown.

As is generally known, Prof. Otto Loewi of Graz, who not long ago shared the Nobel prize with Sir Henry Dale of London, has been deprived of his post and spent some time in custody; he has lately been given his freedom. One of the younger psychiatrists, Prof. Otto Kauders, also of Graz, has been dismissed, ostensibly on racial grounds. Foremost among Viennese psychiatrists and neurologists to be affected by the new régime was Sigmund Freud, who has subsequently been received with great honors in London. Hans Hoff, one of the younger psychiatrists, has emigrated to the United States. Prof. Otto Marburg, ordinarius in neurology, has been deprived of his position; Erwin Stransky has suffered a like fate.

Among the internists who have lost their positions are G. Hitzenberger, radiologist; David Scherf, cardiologist; Julius Bauer, best known for his research on endocrinology and on constitution; Karl Glaessner, Otto Porges and Walter Zweig. The last named was a pupil of Ismar Boas. The tragic death of Professor Boas has previously been reported (THE JOURNAL, August 6, p. 550). The aged man had made Vienna his refuge from Nazi Germany. After the annexation of Austria he ended his life with an overdose of barbital. Still other faculty members to be ousted were Moriz Oppenheim, dermatologist; Gottwald Schwarz, roentgenologist; Josef Friedjung, pediatrician; Richard Wagner and Heinrich Kahr, gynecologists, and Emil Froeschels, research phoniatrician. Prof. Heinrich von Neumann, the otologist, a "non-Aryan," was under arrest until the successful intercession of his patient the duke of Windsor. There have been other suicides in addition to Professor Boas: the aged pediatrician Prof. Wilhelm Knoepfelmacher; 74 year old Prof. Oskar Frankl, gynecologist, and the dermatologist Gabor Nobl, known for his injection therapy of varices. In view of the circumstances this report can make no claim to completeness. It does, however, provide an idea of how the change in the political status of Austria has affected faculties of medicine.

### The Influence of Training on Skeletal Muscles

A. Hoffmann discussed the influence of training on the skeletal muscles before the Berlin Physiologic Society. The current view that muscle responds to any increased demand by hypertrophying is not substantiated by facts. Studies of athletic exercise have demonstrated that muscle adapts itself especially to the exercise by which it is developed; only increased demand within a given unit of time leads to effort hypertrophy, the sum of the exertion (continuous effort performance) having no part in it. According to the observations of Schiefferdecker each muscle possesses, peculiar to itself and to the animal species in question, a ratio of sarcoplasm to the fibrillary substance, size and number of nuclei and so on. This individual character of the muscle is determined by heredity but can be modified according to general health and the demands made on it by the individual. For example, the thickness of the fibers increases in the course of development, whereas the nuclear substance decreases. The microscopic observations of trained muscles are in part contradictory. Schiefferdecker noted in dogs which had undergone a continuous training an enlargement of the fibrous transverse section and a decrease in the number of nuclei; Thörner, on the contrary, in similar studies of dogs, observed no alteration in the thickness of the fibers but an increase in the number of nuclei. Siebert found that in rats forced to perform feats of strength in a definite time the skeletal musculature increased in weight and hypertrophy of the muscle fibers took place. Hoffmann himself performed experiments with thoroughbred Russian rabbits, with the following results: The effort required for different animals to run at various speeds varied greatly, but on the whole the training really amounted to a build-up of endurance. Each of a certain number of animals received, until completion of the experiment, 0.1 Gm. of caffeine per kilogram of body weight. The "caffeine rabbits" were obviously stimulated and displayed greater agility but became fatigued more quickly; these phenomena were particularly remarkable in the speedier rabbits. The spleens of the exercised rabbits were found to weigh in general considerably less than the spleens of the controls, but the spleens of the caffeine rabbits showed no diminution of weight. The hearts of exercised animals weighed more than the hearts of the controls; this increase was even conditioned to a certain extent by the distance traveled. Particular muscles examined were the biceps femoris, the gastrocnemius, the semitendinosus and the soleus. It was found that the muscles of the slow-running animals were always lighter than the muscles of the speedier animals and somewhat heavier than those of the controls; in any case the differences were slight. Increased thickness of the fibers was microscopically observed, together with marked decrease in the number of nuclei. The increase in transverse sections of fiber was accompanied by a corresponding decrease in muscle weight (in the slow-running animals). This phenomenon can be interpreted only by an increase in the muscle at the expense of the fat and of the connective tissue. The increased number of nuclei may be regarded as an economy of a muscle trained to endurance; this phenomenon corresponds with the greater economy of effort observed in other parts of the trained organism.

### Prof. Friedrich von Müller 80 Years Old

Friedrich von Müller, who for many years served as ordinarius of internal medicine at Munich, celebrated his eightieth birthday, September 17. The occasion was recognized in all

scientific and academic circles of Germany. Müller is the last survivor of that group of illustrious men who a few decades ago dominated and determined the development of clinical medicine. Under their guidance the German clinic assumed a preeminent world role and the period of their leadership has already come to be regarded as classic. Friedrich von Müller, the son of a prominent Bavarian physician and hospital director, was during his student days particularly encouraged in scientific thought and endeavor by Carl Voit, one of the founders of classic metabology. Müller received his clinical training from Carl Gerhardt in Würzburg and Berlin. Shortly thereafter Müller came to Bonn, as early as 1890 he was at Breslau as policlinician, in 1892 he was appointed ordinarius at Marburg, in 1899 he became clinical ordinarius at Basel, and in 1903 he succeeded Ziemssen at Munich. His school years and wander years were productive of much work chiefly in the biochemical field: on the absorption of fat, on icterus and urobilin, on metabolism, on disintegration of protein in cancerous patients, on neurologic problems, on exophthalmic goiter, on diagnostic methods. This activity represented the beginning of a great and significant life work. Müller's teaching experience led him to write his famous "Taschenbuch der medizinisch-klinischen Diagnostik," a manual that reappears again and again in new editions and which for fifty years has been and still remains the matchless guide of each new generation of German physicians. This textbook owes its unique position not only to plenitude of material covered in it and the fact that frequent revisions have kept it abreast of contemporary knowledge but also to the extraordinary clarity of presentation. This clarity, this mastery of his subject matter, is notable throughout Müller's published work as well as in his lectures. He has often been invited to speak in foreign countries. His clinical lectures, his world-renowned courses in physical diagnosis always drew large attendance. Müller's lectures always had about them a sterling quality of excellence, they were always marked by a bold highlighting of the essential paths to be explored; he always arrived at the solution of a problem by accurate evaluation of various possibilities. Besides possessing all the qualities of a great physician, Müller has always been a fearless fighter. His impressive lineaments, sharp and angular as if hewn out of wood, are the outward expression of his character, his incorruptible loyalty to the right as he sees it.

## BUDAPEST

*(From Our Regular Correspondent)*

Sept. 20, 1938.

### The Medical Phase of Air Raid Precautions

Dr. Albert Telbisz, organizer of air raid precautions in Hungary, discussed at a recent meeting of the medical society the question as to who is available for medical service in case of gas attacks. Wearing a gas mask causes a change in the mechanism of respiration and circulation. The headband of a well fitting gas mask exerts pressure on the head and in certain persons circulatory troubles and headache supervene. The difficult breathing, profuse sweating, pain, limited sight and fright will disturb medical workers. In a gas-protecting dress the temperature and blood pressure rise, the pulse becomes accelerated, and the loss of body fluid is increased as the result of profuse sweating. The individual worker may collapse.

When a physician selects assistants he must examine them and declare only perfectly healthy subjects fit for air raid service. They must partake in air raid exercises to prepare themselves for this hard work. Some persons feel ill or collapse even during the exercises. This can be explained by the fact that, though they were found healthy, some circulatory disturbance may be latent which, owing to the great muscular effort necessary, suddenly causes decompensation. Dr. Telbisz had occasion to experience this in several cases. Therefore the medical examination should be thorough. When a gas mask is being worn, respiration gradually becomes of the mouth breathing type, particularly if hard work is done; the mucous membrane dries and in consequence an upper prosthesis will fall down in the mouth and hinder breathing and eventually cause suffocation. Persons wearing prostheses should be instructed to take them out of the mouth.

In air raid precaution, physicians have to know what pathologic changes war gases produce in the nonprotected organism. From the pathologic picture he should quickly recognize what poison gas was used. This is important, as efficacious therapy depends on knowing the kind of gas present. There are war gases which produce symptoms that appear only after a latent period of several days. On the other hand, with other gases symptoms speedily supervene.

In planning to protect a hospital, it should be kept in mind that a hospital must always be capable of functioning during and after an aerial attack. A hospital must be independent of all public utilities, having its own water, gas and electric supply and also its own news service. The hospital must be prepared to treat a multitude of injured persons in an air raid. Oxygen inhalation apparatus and oxygen tanks should be handy, with a sufficient stock in storage. Persons exposed to mustard gas must be gas proofed first, and only afterward examined and treated, and gas-proofing stations must be erected within the hospitals.

It is a disputed question whether all hospitals in a threatened area should be evacuated. The answer, says Dr. Telbisz, is no, but only patients recently operated on and not easily transferable should be retained. Particularly important is the evacuation of hospitals which lie in the neighborhood of military barracks, post offices and telephone central exchanges, which will be attacked in case of air raids.

The war gases may affect also the drinking water and food. Water may be contaminated by mustard gas, and food can be soiled also by chlorpicrin. Drinking such water and eating such food may lead to serious consequences.

Telbisz finished his lecture by stating that to organize air raid defense is a difficult task for which experts are wanted.

### Number of Diplomas in Hungary

The faculties of medicine of Hungarian universities issued in the school year 1913-1914 489 new medical diplomas, while in 1935-1936 they issued 398. Considering that in 1913 Hungary's population amounted to 18,000,000 while in 1936 it was only 9,000,000, the 398 diplomas issued in 1936 would seem excessive. In 1917 4,829 physicians practiced in Hungary, and in 1921, in the Hungary which has shrunken almost to one third of its former territory, just as many physicians are practicing. In spite of this, overproduction is not apparent, for now the number corresponds to a rate of one physician to 900 population, which rate would not be excessive if the physicians were better distributed from a geographic point of view. In Budapest itself the rate in 1920 was 1:420, while in 1936 4,460 physicians were registered at the Chamber of Physicians, corresponding to a rate of 1:239. In 1920 it was about 3,000 persons to one physician in the rural districts while in 1936 the number of rural physicians almost doubled and the rate became 1:1,412. In 2,317 of 3,374 villages there are no physicians. There are villages having a population of more than 3,000 with no physician.

In the cities, and especially in the capital city, the ever spreading sickness insurance endangers private practice. A grave problem is the question of free medical work. The reform of medical attendance on poor patients, contemplated by the ministry of health, will probably solve this question. The minister holds that a physician can work best only if his livelihood is assured, and therefore assuring their livelihood is no private affair of the medical profession but a public health matter. According to statistics issued by the bureau of taxa-

tion, of 8,451 practitioners 186 did not earn 200 pengos, or $60; almost every fifth doctor earns less than 500 pengos, or $150 yearly; 42 per cent did not reach 1,000 pengos yearly, or $300, and only 28 per cent made 10,000 pengos, or $3,000. The income of the most popular physicians did not exceed 60,000 pengos, or $18,000. The so-called Aid for Young Physicians endeavors to deviate young doctors from the capital and to grant loans to village doctors until they can maintain themselves. These subsidies need not be repaid.

### Typewritten Medical Prescriptions

The representatives of the Czechoslovakian Medical and Pharmaceutical Chambers discussed the problem of the legibility of medical prescriptions, since pharmaceutic chemists complained to the board that they often get prescriptions which are utterly illegible. As a consequence, the medical chambers require their members to write their prescriptions legibly. Those having such illegible handwriting must use typewriters.

## ITALY

*(From Our Regular Correspondent)*

Oct. 1, 1938.

### Meeting of Anesthetists

The Società italiana di anestesia e analgesia met recently in Bologna, with Professor Dogliotti as president. The first official topic was "Criteria for Selection of Anesthesia." Professor Gianotti concluded that preanesthesia is of value as complemental to ether and gas anesthesia. Basal (intravenous and rectal) anesthesia is of value but, in the majority of cases, cannot be a substitute for anesthesia by inhalation. Intravenous, rectal and chloroform anesthesia interfere with the functions of the liver and the kidney more than ether anesthesia. Use of the latter is especially indicated in children as well as in patients with syphilis, meningitis, mental or nervous disorders, infections with septicemia and shock. Ether and chloroform anesthesia aggravate acidosis. Gas anesthesia is harmless to the parenchymal organs. However, its administration is difficult because of the necessary apparatus and technic. Spinal anesthesia is contraindicated in hypotension as well as in all conditions in which ether anesthesia is indicated. Persons of the macrosplanchnic type tolerate spinal and peridural anesthesia better than those of other types. Peridural anesthesia is more advisable than high subarachnoid anesthesia. The latter, especially if nupercaine is used, may be followed by immediate or late complications. Nupercaine has to be used in small doses when it is used for local anesthesia in patients in poor nutritional conditions or in those who are suffering from pathologic conditions of either the liver or the kidney.

Professor Gosset reported satisfactory results from cyclopropane anesthesia in 467 cases. The toxicity of cyclopropane is low and when mixed with oxygen in the proportion of 22 per cent it induces anesthesia with loss of the reflexes. According to Weese's opinion, based on results of experiments, the complications which follow operations on phlegmons of the mouth are caused by changes of respiratory reflexes which originate in the carotid sinus.

Professors Trincas and Oggioni reported experimental results obtained with Donaggio's method. Donaggio, in the course of the Congress of the Società di anestesia e analgesia which took place in 1936, said that he succeeded in showing the microscopic changes which anesthesic substances cause on the nerve fibers. He used a special method of fixation and coloration in making the microscopic preparations. The pathologic changes have the characteristics of the initial phase of primary degeneration. Professors Trincas and Oggione studied, by means of Donaggio's method, the action of procaine hydrochloride, nupercaine, tutocain and prexocaine on the fibers of the cervical sympathetic. Procaine hydrochloride, nupercaine and tutocain have a selective action on the neuraxis. Prexocaine attacks the myelinic sheath.

Professor Ruggeri made a chart on the gradation of changes induced by cocaine, stovaine (amylocaine hydrochloride, B. P.), procaine hydrochloride, tutocain and pantocain on the fibers of the sciatic nerve. The most grave changes are those induced by pantocain and procaine hydrochloride.

The second official topic was "Anesthesia with Heated Ether Vapor." Professor Parenti said that by heating ether vapors and administering them under high tension they acquire the characteristics of a gas less toxic and more active than ether. With D'Agostino's apparatus the patients inhale heated ether vapors and at the same time they inhale a mixture in which the amount of air, the expired carbon dioxide and the water vapor can be controlled. The speaker found, by clinical investigations, that heated ether vapors reach the respiratory tract of the patients at a temperature of 18 or 20 C. (64.4 to 68 F.). He found by experiments on animals that during administration of anesthesia by means of D'Agostino's apparatus the air is quickly regulated at the first segments of the respiratory tract and is maintained at a constant temperature in the tracheobronchopulmonary system. The speaker has found on microscopic study that normal ether vapors harm the respiratory tract more than the heated ones. The latter enter the blood in smaller proportions and are more quickly eliminated than the former. Professor Giordanengo showed a device of his own which can be attached to the common masks to obtain heating of anesthetic vapors.

## Marriages

William Larkin Norville, Whitmire, S. C., to Miss Lillie Mae Freeman of Rutherfordton, N. C., June 3.

William Bertram Martin, Warrior, Ala., to Miss Emily Francis Johnson of Birmingham in August.

Raymond Francis Smith to Dr. Janith Stewart Kice, both of Garden City, N. Y., July 20.

Sol Stein Kaufman, Rayne, La., to Miss K. Yelverton of Mize, Miss., at Bunkie, La., June 2.

John K. Burns, Spokane, Wash., to Miss Neva L. Palmer of Klamath Falls, Ore., August 25.

Joseph Nagle, Portsmouth, Va., to Miss Jane Elizabeth Montgomery of Norfolk, July 19.

Edward A. Kuehn, Vandalia, Ill., to Miss Marguerite Robbie of Cedar Rapids, Iowa, August 8.

John B. Alseven, Syracuse, N. Y., to Miss Janet Gilbert of Springfield, Mass., August 27.

William Niles Wishard Jr. to Miss Carolyn Louise Davis, both of Indianapolis, October 10.

Marshall H. Aiken, Tiffin, Ohio, to Mrs. Hester Witbeck Ross of Sandusky, August 28.

Thomas Hamilton Brem, Baltimore, to Miss Emily E. Bloss of Roselle, N. J., August 27.

Alva M. Kirkpatrick to Miss Esther Whitson, both of Columbus, Ind., in August.

Richard van Dyck Knight to Miss Jane Wyeth, both of New York, September 3.

Charles J. Kistler, Kingston, Pa., to Miss Marjorie Bone of Nanticoke, June 12.

Harvey G. E. Mallow to Miss Alice Dierker, both of Watertown, Wis., July 21.

John M. Brecht to Miss Margaret R. Shank, both of Norristown, Pa., June 18.

Joseph L. Kruszewski to Miss Sophie Taczala, both of Milwaukee, July 6.

William H. Frackelton to Miss Jane Love, both of Milwaukee, June 18.

Raymond J. Kokowicz to Miss Irene R. Rozycki, both of Detroit, in June.

Robert J. Porter to Miss Jean Beyer, both of Des Moines, Iowa, June 16.

# Deaths

**Henry Martyn Bracken** ● secretary and executive officer of the Minnesota State Board of Health from 1897 to 1919, died, September 25, at his home in Claremont, Calif., of chronic myocarditis, aged 84. Dr. Bracken was born in Noblestown, Pa., Feb. 27, 1854. He received the medical degree from the College of Physicians and Surgeons, Medical Department of Columbia College, New York, in 1877, and was a licentiate of the Royal College of Surgeons of Edinburgh, Scotland, in 1879; then for three years he was a ship surgeon. On the organization of the Medical College of the University of Minnesota in 1887 Dr. Bracken was appointed professor of materia medica and therapeutics. He lectured on public health and preventive medicine and for a time was acting dean of the medical college from which he resigned in 1907 to give his time to the state board of health. Dr. Bracken was appointed a member of the state board of health in 1895 and was elected secretary and executive officer in 1897. In 1902 he was president of the Conference of State and Provincial Health Authorities of North America and from 1908 to 1913 secretary-treasurer. He was a member of the first board of directors of the National Tuberculosis Association. In 1906 he organized the Minnesota Association for the Prevention and Relief of Tuberculosis, now the Minnesota Public Health Association. He also organized the Minnesota State Sanitary Conference and was its secretary. In 1919, Dr. Bracken was commissioned in the reserve corps of the United States Public Health Service as surgeon and was assigned to the Veterans' Bureau. He resigned in 1923. He was a member of the Minnesota State Medical Association, International Congress of Hygiene and Demography, International Congress of Tuberculosis, Royal Sanitary Institute, England, and the American Association for the Study and Prevention of Infant Mortality, honorary vice president of the fourth International Congress on School Hygiene and past president of the American School Hygiene Association. He was at one time attending physician to the Asbury Hospital and St. Barnabas Hospital in Minneapolis. Dr. Bracken was secretary of the Section on Hygiene and Sanitary Science of the American Medical Association, 1901-1902, and chairman, 1902-1903, and member of the Council on Health and Public Instruction from the time of its organization in 1910 until the 1919 session.

**John Roberts Caulk** ● St. Louis; Johns Hopkins University School of Medicine, Baltimore, 1906; professor of clinical genito-urinary surgery, Washington University School of Medicine; member of the Southern Surgical Association and the Clinical Society of Genito-Urinary Surgeons; past president of the American Urological Association and the American Association of Genito-Urinary Surgeons; fellow and member of the board of governors of the American College of Surgeons; served in various capacities on the staffs of the Barnes Hospital, St. Louis Maternity Hospital, St. Luke's Hospital, St. Louis Children's Hospital, Jewish Hospital, Evangelical Deaconess Home and Hospital and St. Louis County Hospital; contributor of chapters to Cabot's "System of Urology," Bartlett's "Post-Operative Surgery," Lewis' "Surgery" and "Cyclopedia of Practical Medicine"; aged 56; died, October 13, in Clayton, Mo.

**Alexander Fraser,** New York; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1897; member of the Medical Society of the State of New York; formerly professor of pathological histology at the University and Bellevue Hospital Medical College, and professor of pathology and bacteriology at the New York Polyclinic Medical School and Hospital; pathologist to St. Vincent's Hospital, consulting pathologist and bacteriologist to the New York Polyclinic Hospital, consulting pathologist at the New York Foundling Hospital, and the Manhattan Maternity Hospital, New York, and the Monmouth Memorial Hospital, Long Branch, N. J.; aged 69; died, September 18 at his summer home in Beechurst, L. I., of acute cholangitis.

**Arthur Everett Austin,** Boston; Harvard University Medical School, Boston, 1887; fellow of the American College of Physicians; professor of theory and practice of medicine, emeritus, Tufts College Medical School; formerly professor of biochemistry at the University of Virginia, and the University of Texas, Galveston; formerly on the staffs of the Mount Sinai Hospital and the Massachusetts General Hospital; served during the World War; author of "Manual of Clinical Chemistry" and "Diseases of the Digestive Tract and Their Treatment"; aged 77; died, August 22, in Windham, N. H.

**Harvey Ward Van Allen** ● Springfield, Mass.; Albany (N. Y.) Medical College, 1891; member of the House of Delegates of the American Medical Association, 1912-1913; member of the American Roentgen Ray Society, New England Roentgen Ray Society and the Radiological Society of North America; president of the American College of Radiology; on the staffs of the Springfield and Wesson hospitals, Mary Lane Hospital, Ware, and Cooley-Dickinson Hospital, Northampton; aged 69; died, August 2, of coronary thrombosis and cerebral embolism.

**Golder Lewis McWhorter** ● Chicago; Rush Medical College, Chicago, 1913; associate clinical professor of surgery at his alma mater; member of the Western Surgical Association; fellow of the American College of Surgeons; served during the World War; on the staffs of the Presbyterian Hospital, Oak Forest Infirmary and Cook County Hospital; author of numerous surgical papers, especially on the gallbladder and gastrointestinal tract; aged 50; died, October 16, of retroperitoneal sarcoma and uremia.

**Frank Clifford Ard,** Westfield, N. Y.; University of Maryland School of Medicine, Baltimore, 1887; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; formerly on the staffs of the Muhlenberg Hospital, Plainfield, N. J., Somerset Hospital, Somerville, N. J., and the Bonnie Burn Sanatorium, Scotch Plains, N. J.; aged 74; died, August 23, of arteriosclerotic heart disease and aneurysm.

**John Dillon Stewart** ● New York; Medical College of Indiana, Indianapolis, 1905; professor of clinical surgery at the New York Post-Graduate Medical School, Columbia University; member of the American Proctologic Society; fellow of the American College of Surgeons; aged 57; on the staffs of the Bushwick Hospital, Brooklyn, and the New York Post-Graduate Hospital, where he died, August 3, of subacute bacterial endocarditis.

**Allan Rupert Cunningham,** Halifax, N. S., Canada; Dalhousie University Faculty of Medicine, Halifax, 1904; assistant professor of diseases of the eye at his alma mater; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; on the staff of the Victoria General Hospital; aged 50; died, July 3, of pulmonary tuberculosis.

**Walter Freeman Taylor** ● Dallas, Texas; University of Louisville (Ky.) School of Medicine, 1930; an Associate Fellow of the American Medical Association; associate professor of biochemistry and chemical pathology at Baylor University College of Medicine; served during the World War; aged 47; died, August 7, of coronary thrombosis.

**Charles A. Hall,** Cleveland; Homeopathic Hospital College, Cleveland, 1888; Cleveland College of Physicians and Surgeons, Medical Department of Ohio Wesleyan University, Cleveland, 1899; fellow of the American College of Surgeons; for many years on the staff of St. John's Hospital; aged 74; died, August 19, of tetanus and bronchopneumonia.

**George A. Tripp** ● South Bend, Wash.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; fellow of the American College of Surgeons; secretary of the Pacific County Medical Society; formerly county health officer; one of the medical directors of the Pacific General Hospital; aged 66; died, August 11.

**Robert Dannelly Schimmelpfennig** ● Montclair, N. J.; Tulane University of Louisiana School of Medicine, New Orleans, 1908; member of the Radiological Society of North America; served during the World War; on the staff of the Mountainside Hospital; aged 56; died, August 10, in Belmar of coronary occlusion.

**Howard Clyde Rockwell** ● Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; formerly secretary of the Ingham County Medical Society; editor of the *Bulletin of the Ingham County Medical Society*; aged 51; died in August of carbon monoxide poisoning, self administered.

**Edville Gerhardt Abbott,** Portland, Maine; Medical School of Maine, Portland, 1898; member of the Maine Medical Association; fellow of the American College of Surgeons; on the staffs of the Maine General Hospital and the Children's Hospital; aged 66; died, August 27, of coronary occlusion.

**John Burton Ro Bards,** Harrodsburg, Ky.; Hospital College of Medicine, Louisville, 1897; member of the Kentucky State Medical Association; served during the World War; member of the school board; formerly member of the state legislature; aged 68; died, August 11, of angina pectoris.

**Owen Wynne Butler** ● Nicholasville, Ky.; University of the City of New York Medical Department, 1894; member of the Missouri State Medical Association; aged 73; died, August 11, in the Good Samaritan Hospital, Lexington, of carcinoma at the ampulla of vater and subdiaphragmatic abscess.

**Ben Hill Turner,** Cleburne, Texas; Louisville (Ky.) Medical College, 1904; member of the State Medical Association of Texas; past president of the Johnson County Medical Society; county health officer; on the staff of the Cleburne Sanitarium; aged 62; died, August 12, of coronary occlusion.

**Charles Hewitt Randall,** Newark, N. J.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; member of the Medical Society of New Jersey; aged 73; died, August 3, in the Newark City Hospital of arteriosclerosis and cerebral hemorrhage.

**Sylvester Edward Ryan** ● Springfield, Mass.; Columbia University College of Physicians and Surgeons, New York, 1905; served during the World War; on the staff of the Mercy Hospital; aged 56; died, August 9, at his home in Longmeadow of hypertension and coronary thrombosis.

**Homer Allen Walkup** ● Mount Hope, W. Va.; Medical College of Virginia, Richmond, 1914; past president and secretary of the Fayette County Medical Society; at one time city health officer; aged 49; died, August 19, in the Laird Memorial Hospital, Montgomery, of myocarditis.

**Charles Shanks,** New Bedford, Mass.; Harvard University Medical School, Boston, 1903; member of the Massachusetts Medical Society; served during the World War; formerly medical inspector in the city schools; aged 59; died, August 2, of carcinoma of the intestine.

**Axel Wilhelm Swedenburg** ● Thief River Falls, Minn.; Chicago College of Medicine and Surgery, 1907; served during the World War; formerly on the staff of the Physicians Hospital; aged 65; died, August 20, of cerebral hemorrhage and arteriosclerosis.

**Charles Delbert Snively,** Ipava, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1897; served during the World War; member of the Illinois State Medical Society; secretary of the Fulton County Medical Society; aged 63; died, August 2, of heart disease.

**Harrison Christian Riegel,** Kecoughtan, Va.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; aged 60; on the staff of the Veterans Administration Facility, where he died, August 5, of heart disease.

**Thomas Shirley Venard** ● Ness City, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; veteran of the Spanish-American and World wars; aged 62; died, August 29, of chronic myocarditis.

**William Hervey Albright,** Alpha, N. J.; Medico-Chirurgical College of Philadelphia, 1899; for many years member and secretary of the board of education; aged 72; died, August 7, in the Easton (Pa.) Hospital of cerebral hemorrhage.

**Edward J. Brennan,** Indianapolis; University of Buffalo School of Medicine, 1871; aged 86; honorary member of the staff of St. Vincent's Hospital, where he died, August 2, of chronic myocarditis and arteriosclerosis.

**Everette Majjette Leake,** Norfolk, Va.; University of Maryland School of Medicine, Baltimore, 1926; on the staff of the Leigh Memorial Hospital; aged 37; died, August 8, of hypertension and cerebral hemorrhage.

**Frank Marion Fitch** ● Indianapolis; Medical College of Indiana, Indianapolis, 1904; for many years on the staff of the Methodist Episcopal Hospital; aged 63; died suddenly, August 21, of chronic myocarditis.

**Mason Combs,** Pineville, Ky.; Hospital College of Medicine, Louisville, 1905; served during the World War; aged 55; died, August 31, in the Veterans' Administration Facility, Lexington, of coronary occlusion.

**Ivy W. Moorman,** Douglas, Ga.; University of Georgia Medical Department, Augusta, 1897; member of the Medical Association of Georgia; aged 70; died, August 10, of coronary thrombosis and diabetes mellitus.

**Carl Schurtz,** Streator, Ill.; Marion-Sims College of Medicine, St. Louis, 1900; member of the Illinois State Medical Society; aged 62; died, August 13, in St. Mary's Hospital following a gallbladder operation.

**Roy Raymond Miller,** Mound City, Mo.; Ensworth Medical College, St. Joseph, 1905; member of the Missouri State Medical Association; aged 55; died, August 6, of nephritis, hypertension and heart disease.

**Edward Marquette Harrington,** Chicago; Northwestern University Medical School, Chicago, 1924; member of the Illinois State Medical Society; aged 40; died, August 22, in Peoria, of coronary occlusion.

**James Eugene Pritchard,** Aurora, Ill.; Washington University School of Medicine, St. Louis, 1908; member of the Illinois State Medical Society; aged 52; died, August 6, of amyotrophic lateral sclerosis.

**Tharos Harlan,** Auburn, W. Va.; George Washington University School of Medicine, Washington, D. C., 1905; at one time served in various capacities with the U. S. Navy; aged 58; died, August 2, of angina pectoris.

**William B. Fuqua,** Radford, Va.; University College of Medicine, Richmond, 1897; member of the Medical Society of Virginia; for many years city coroner; aged 64; died, August 18, of cerebral hemorrhage.

**George W. King,** Charlevoix, Mich.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1906; member of the Michigan State Medical Society; aged 70; died, August 22, of uremia following pyelitis.

**Alexander Hamilton S. Rouss,** Charles Town, W. Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1906; served during the World War; aged 56; died, August 28, of myocarditis.

**Claudius Abijah Hayworth,** Asheboro, N. C.; University of Maryland School of Medicine, Baltimore, 1913; aged 55; died, August 5, in a hospital at Winston-Salem of cirrhosis of the liver and diabetes mellitus.

**Jerome Josephus Stout,** Dayton, Ohio; Ohio Medical University, Columbus, 1902; member of the Ohio State Medical Association; aged 61; died, August 25, at the Miami Valley Hospital of heart disease.

**Walter Scott Keyting,** Salt Lake City; University of Pennsylvania School of Medicine, Philadelphia, 1912; member of the Utah State Medical Association; aged 51; died, August 8, of coronary thrombosis.

**Robert Benjamin Porter** ● Glenwood Springs, Colo.; Denver and Gross College of Medicine, 1906; medical director of a hospital bearing his name; aged 58; died, August 11, of cardiovascular disease.

**John Mortimer Crawe** ● Watertown, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; aged 75; died, August 13, of acute nephritis and uremia.

**Clarence Starr Cutter,** Cleveland; Cleveland Medical College, 1894; aged 70; on the staff of the Glenville Hospital, where he died, August 19, of influenza, bronchopneumonia and cerebral embolus.

**William Simeon Miller,** Estelline, Texas; University of Louisville (Ky.) Medical Department, 1881; member of the State Medical Association of Texas; aged 79; died, August 17, of endocarditis.

**Franklin T. Poehler,** Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1896; aged 66; died, August 3, in the General Hospital of a self-inflicted bullet wound.

**Eugene R. Smith,** Andalusia, Ala.; Maryland Medical College, Baltimore, 1904; member of the Medical Association of the State of Alabama; aged 59; died, August 25, of cerebral hemorrhage.

**William Canfield Dean,** Jericho, N. Y.; University of the City of New York Medical Department, 1897; aged 61; died, August 21, in the Nassau Hospital, Mineola, of gastrointestinal hemorrhage.

**Robert Lester Allen,** Haskell, Okla.; University of Arkansas School of Medicine, Little Rock, 1905; aged 65; died, August 31, of hypertension, arteriosclerosis and cerebral hemorrhage.

**Charles Wesley Froedge,** Glasgow, Ky.; University of Louisville Medical Department, 1893; member of the Kentucky State Medical Association; aged 72; died, August 7, of coronary thrombosis.

**David Nicholas Schaffer,** Evanston, Ill.; Loyola University School of Medicine, Chicago, 1916; aged 52; died, August 24, in the Westlake Hospital, Melrose Park, of adenocarcinoma of the rectum.

**Walter N. John** ● Hugo, Okla.; University of Texas School of Medicine, Galveston, 1894; formerly county health officer; aged 67; died, August 15, in the Sanitarium of Paris, Texas, of carcinoma.

**Harry Lent Russell,** Newark, N. J.; Hahnemann Medical College and Hospital, Chicago, 1901; aged 71; died, August 21, in the Newark Convalescent Hospital of coronary occlusion and empyema.

**Charles F. Culver,** Howell, Mich.; Jefferson Medical College of Philadelphia, 1900; member of the Michigan State Medical Society; aged 67; died, August 19, of coronary occlusion.

**Herbert Benjamin Wren** ● Shreveport, La.; Memphis (Tenn.) Hospital Medical College, 1900; aged 65; died, August 11, in the Tri-State Hospital of carcinoma of the prostate.

**William Jacob Rabenau,** Springfield, Mo.; Missouri Medical College, St. Louis, 1885; member of the Missouri State Medical Association; aged 80; died, August 26, of chronic nephritis.

**William J. Harrell,** Elkville, Ill.; Memphis (Tenn.) Hospital Medical College, 1883; past president of the high school board of education; aged 78; died, August 21, of cerebral hemorrhage.

**Abraham Frank,** Philadelphia; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1901; aged 67; died, August 17, in Atlantic City, N. J., of cardiac decompensation.

**Albert Henry Parks,** Minneapolis; Northwestern University Medical School, Chicago, 1906; member of the Minnesota State Medical Association; aged 58; hanged himself, August 30.

**Ollie Thomas Lowery** ● Tolu, Ky.; University of Louisville Medical Department, 1907; served during the World War; aged 55; was accidentally shot and killed, August 7.

**Benjamin Harrison Gibson,** Allenhurst, Ga.; University of Maryland School of Medicine, Baltimore, 1909; member of the Medical Association of Georgia; aged 51; died, August 3.

**Spero G. Bicatos Vryonis,** Bridgeport, Conn.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1912; aged 54; died, August 9, in Athens, Greece, of heart disease.

**Caroline Frances Brooks Woodruff,** Independence, Iowa; Boston University School of Medicine, 1884; aged 86; died, August 20, of an injury of the hip received in a fall.

**John A. McCulloch** ● Maryville, Tenn.; University of Tennessee Medical Department, Nashville, 1901; aged 62; died, August 12, in Knoxville, of coronary sclerosis.

**Edward Chambers Laird,** Morehead City, N. C.; University of Maryland School of Medicine, Baltimore, 1877; aged 83; died, August 21, of uremia and nephritis.

**Finley P. Johnson,** Hoopeston, Ill.; Rush Medical College, Chicago, 1885; aged 82; died, August 8, in the Lake View Hospital, Danville, of bronchopneumonia.

**Gerald Andrew Scully** ● Silver Spring, Md.; Georgetown University School of Medicine, Washington, D. C., 1927; aged 38; died, August 29, of aplastic anemia.

**William Luther Cameron,** Lincoln, Neb.; Drake University College of Medicine, Des Moines, Iowa, 1887; aged 83; died, August 14, of Addison's disease.

**Frank Harold Boyd,** Allendale, S. C.; University of Georgia School of Medicine, Augusta, 1892; aged 68; died, August 9, of pulmonary tuberculosis.

**Albert Elmer Derwent,** Clinton, Mo.; Rush Medical College, Chicago, 1897; aged 77; died, August 27, in the Research Hospital, Kansas City, of pneumonia.

**John Louis Snow,** Montgomery, Ala.; Medical College of Alabama, Mobile, 1891; aged 70; died, August 3, of arteriosclerosis and cerebral hemorrhage.

**David Cameron Murray,** Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1904; aged 63; died, August 14, in Campbellton, N. B.

**Carig Tipton Lewis,** McKinney, Texas; Kentucky School of Medicine, Louisville, 1900; aged 78; died, August 7, in the City Hospital of lobar pneumonia.

**George T. Williamson,** Ellenwood, Ga.; Southern Medical College, Atlanta, 1893; formerly bank president; aged 75; died, August 17, of chronic myocarditis.

**John B. Conkling,** Cooperstown, N. Y.; Eclectic Medical Institute, Cincinnati, 1883; aged 78; died, July 18, of cerebral hemorrhage and arteriosclerosis.

**Charles Augustus Dennett** ● Sebago, Maine; Medical School of Maine, Portland, 1888; aged 75; died, August 11, in Portland of cerebral thrombosis.

**George Archibald Hutchinson,** Capron, Ill.; Northwestern University Medical School, Chicago, 1909; aged 53; died, August 4, of injuries received in a fall.

**David L. Gaillard,** Greenville, Texas; Louisville (Ky.) Medical College, 1877; aged 84; died, August 24, following an operation for thyroid disease.

**Joseph Shingleman** ● Cicero, Ill.; Illinois Medical College, Chicago, 1909; formerly city health officer; aged 58; died, August 7, of angina pectoris.

**Clarence Snyder,** Arcadia, Ohio; University of the South Medical Department, Sewanee, Tenn., 1894; aged 67; died, August 7, of arteriosclerosis.

**Henry Homer Black,** London, Ont., Canada; Western University Faculty of Medicine, London, 1906; aged 63; died, August 10, of heart disease.

**Adolf George Kaumeyer,** Maybee, Mich.; Michigan College of Medicine and Surgery, Detroit, 1897; aged 64; died, August 2, of heart disease.

**Albert T. Washburn,** Taylorville, Ill.; Chicago Homeopathic Medical College, 1891; aged 67; died, August 5, in Edinburgh of heart disease.

**Fred E. Calkins,** Fremont, Neb.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1899; aged 72; died, August 28, of uremia.

**M. Hugh Cobb,** Thomasville, Ga.; Meharry Medical College, Nashville, Tenn., 1897; aged 69; died, August 28, in Quitman of heart disease.

**Dudley W. Lane,** Philadelphia; Jefferson Medical College of Philadelphia, 1882; aged 79; died, July 20, of acute dilatation of the heart.

**Arthur Frank Kleykamp,** St. Louis; Washington University School of Medicine, St. Louis, 1902; aged 58; died, August 26, of pneumonia.

**James Scott Cummings,** Bronson, Kan.; Cincinnati College of Medicine and Surgery, 1880; aged 86; died, August 26, of myocarditis.

**Angus Maybin Ferguson,** Deming, N. M.; Medical College of Alabama, Mobile, 1903; aged 61; died, August 5, of heart disease.

**William J. C. Casely,** Marengo, Ill.; Chicago Medical College, 1885; aged 76; died, August 2, of atrophic cirrhosis of the liver.

**Norvin G. Perry Sr.,** Worthville, Ky.; Miami Medical College, Cincinnati, 1871; aged 92; died, August 21, of cerebral hemorrhage.

**Timothy Joseph Cullinane,** Andover, Mass. (licensed in Massachusetts in 1906); aged 58; died, August 14, of chronic myocarditis.

**George R. Jones,** Galena, Md.; Atlantic Medical College, Baltimore, 1907; aged 57; died, August 27, of heart disease and nephritis.

**William Warner Wentworth,** New York; Albany (N. Y.) Medical College, 1893; aged 69; died, August 16, in St. Vincent's Hospital.

**George W. Hous,** Dayton, Ohio; Medical College of Ohio, Cincinnati, 1877; aged 89; died, August 7, of heart disease and nephritis.

**P. L. Froeland,** Proctor, W. Va.; Hospital College of Medicine, Louisville, Ky., 1889; aged 75; died, August 22, of coronary sclerosis.

**John W. Snider,** Fairland, Ind.; Rush Medical College, Chicago, 1870; aged 93; died, August 6, of pulmonary tuberculosis.

**T. Lester Jones** ● Lansing, N. C. (licensed in North Carolina in 1909); aged 54; died, August 1, of diabetes mellitus.

**Frederick James Colling,** Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1901; died, August 13.

**Andrew Hyden,** Alcester, S. D.; Keokuk (Iowa) Medical College, 1894; aged 75; died, August 21, of pernicious anemia.

**Lloyd L. Hall** ● Youngstown, Ohio; Baltimore Medical College, 1902; aged 62; died, August 1, of coronary occlusion.

**Joseph Luther Sheppe,** Huntington, W. Va.; Maryland Medical College, Baltimore, 1907; aged 82; died, August 24.

**Loyd M. Bell,** Pataskala, Ohio; Toledo Medical College, 1885; aged 79; died, August 16, of cerebral hemorrhage.

**Frank S. Peck,** Oklahoma City; St. Louis Eclectic Medical College, 1874; aged 97; died, August 14, of senility.

**Luther Howard Cartledge,** Atlanta, Ga.; Southern Medical College, Atlanta, 1882; aged 82; died in August.

**Robert Leighton Island,** Toronto, Ont., Canada; Trinity Medical College, Toronto, 1880; died, August 14.

**Kansas D. Davis,** Chattanooga, Tenn.; Atlanta Medical College, 1881; aged 81; died, August 13.

**James Grant McKenzie,** Paragould, Ark. (licensed in Arkansas in 1903); died, August 10.

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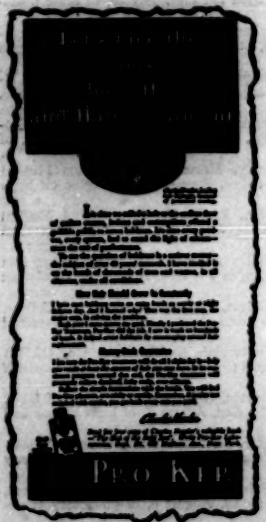
## Bureau of Investigation

### PRO-KER LABORATORIES, INC.

**The Mails Are Closed to a "Hair Replacement" Scheme**

The Pro-Ker Laboratories, Inc., was a concern that sold through the mails a "treatment" called "Pro-Ker Hair Milk" which, it was claimed, would prevent premature baldness and replace falling hair. The business was incorporated in New York in 1932. In March of this year the concern was called on to show cause why a fraud order should not be issued against it and its officers, as such. On April 4 the president of the concern, Charles G. Nessler, accompanied by an attorney, appeared in Washington and a hearing was held. On June 24, after going over all the evidence in the case and also considering a brief submitted by the concern's attorney, the Acting Solicitor for the Post Office Department, the Hon. W. E. Kelly, recommended to the Postmaster General that a fraud order be issued. The order was issued on June 30, 1938.

As long ago as August 1936 the Federal Trade Commission issued a complaint against the Pro-Ker Laboratories, Inc., charging that the advertisements which represented Pro-Ker as a competent treatment for baldness were false. The commission, however, did not issue an order for the company to cease its false statements until Sept. 9, 1938—more than two months after the Post Office officials had closed the mails to it.




The Pro-Ker Laboratories, Inc., caught its suckers with the usual bait: newspaper advertisements. The company was incorporated by the father of the president of the concern, Charles Nessler senior, who, it has been claimed, was the inventor of the "permanent wave." In 1927 Nessler senior published a book entitled "The Story of Hair." The reviewers seem to have given it a "good press," judging from the excerpts published by Nessler in promoting Pro-Ker. Such favorable reviews will not surprise those familiar with the close community of interest between the book review departments and the advertising offices of some newspapers.

In its advertisements the Pro-Ker Laboratories, Inc., urged the public—at least that part of the public which feared loss of hair—to send for its free booklet "The End of the Bald Era." Even such a careful and conservative paper as the New York *Times Magazine* carried a full page advertisement of the booklet in its issue of Nov. 13, 1932. Those who sent for the booklet were told that the secret of "hair replacement" lay in the use of Pro-Ker, which the company described as "Hair Milk," together with the following of certain directions regarding the care of the scalp.

Pro-Ker was analyzed for the Post Office Department by the chemists of the Food and Drug Administration of the Department of Agriculture. They reported:

> "The product is a milky liquid with a lavender-like odor and a soapy taste. It consists of a small amount of sodium sulfate [Glauber's Salt, sometimes called Horse Salt, because used by veterinarians] and a small amount of fatty oil emulsified in water by means of a soap—a sulfonated oil soap is indicated. A small amount of formaldehyde is present and also traces of volatile oils, among which oil of lavender is indicated."

Two physicians testified on behalf of the government at the hearing at Washington, but the Nessler concern did not present any witnesses at all. In the brief submitted by the Nessler attorney after the hearing it was contended that the action of the Post Office was obnoxious to the Fifth Amendment to the Constitution of the United States and constituted a deprivation of property without due process of law! Such a contention was wholly without foundation, as the postal fraud order laws have been held constitutional repeatedly by the United States Supreme Court. The brief also charged that the action of the postal authorities was an attack "aimed at the *theories* and *opinions* of Charles Nessler." Acting Solicitor Kelly, in his memorandum to the Postmaster General, pointedly replied that Nessler's counsel had entirely missed the point; that the proceedings in the case were directed not at the theories and opinions of Nessler but against the false and fraudulent pretenses, representations and promises contained in the written and printed matter that the Pro-Ker Laboratories, Inc., sent through the United States mails. Mr. Kelly further emphasized that a person who has made false and fraudulent claims "as to the curative properties of a treatment which he is selling cannot, when pursued by justice, take refuge in the statement that he was expressing his opinion."

The memorandum to the Postmaster General also brings out the fact that purchasers of Pro-Ker bought the product on the representation, among others, that it would retain on the scalp of the user at least the same amount of hair which existed when the treatment was started or, alternatively, would reestablish the amount of hair within seven months and arrest further hair loss. The facts were, said Mr. Kelly, that Pro-Ker did not and could not achieve such a result.

As previously stated, the fraud order against the Pro-Ker Laboratories, Inc., and its officers and agents as such, was issued June 30, 1938.

### TUBRON

**The Fraudulent Consumption Cure of H. G. Haring**

Henry G. Haring, a druggist who conducted a small drug store in Philadelphia, sold through the mails a preparation called "Tubron" or "Tubron (Haring)" as a treatment for the cure of tuberculosis. Haring obtained his victims by advertising in certain newspapers that were not above sharing the profits to be made by swindling consumptives.

When Haring was called on by the Post Office officials to show cause why a fraud order should not be issued against him, a written answer was submitted by an attorney who indicated that if the enterprise were found to be an improper one his client would discontinue it. The postal authorities thereupon furnished the respondent with a form of affidavit providing for the discontinuance of the enterprise. But Haring refused to execute the affidavit!

According to the evidence in the case, Haring claimed that "after 30 years of study, research, experiment, application and observation" he had perfected a remedy for tuberculosis. He declared that, while good food, rest and fresh air were "good adjuncts" to the treatment of tuberculosis, "Tubron" was "the essential treatment." When analyzed by government chemists, Tubron was found to be essentially an emulsion of cod liver oil and hypophosphites with small amounts of strychnine, oil of wintergreen, alcohol and water. The amount of cod liver oil found was much too small for any practical purpose and the mixture might in many instances prove harmful because it would upset the digestion.

In his memorandum to the Postmaster General, recommending the issuance of a fraud order, the acting solicitor for the Post Office Department, the Hon. W. E. Kelly, brought out the fact that Haring's "patent medicine" was worthless and was not, as claimed, a "rapid and permanent cure" for tuberculosis. It was declared too that Haring's scheme was a fraudulent one and urged that the mails be closed to Haring's Pharmacy, H. G. Haring and the West Philadelphia Tuberculosis Dispensary. On July 1, 1938, the fraud order was issued and the mails closed to these names, as recommended.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## TREATMENT OF DOG BITE

*To the Editor:*—I recently noted the correspondence in THE JOURNAL relative to the treatment of dog bite with fuming nitric acid. Will you please explain the rationale of this treatment? Is there any record of rabies ever having been prevented with this treatment following the bite of a proved rabid dog without the use of the Pasteur treatment? Is it not true that the only treatment of any avail whatever is the Pasteur treatment or a modification of it? If this is true, why should the patient be subjected to the discomfort and probable scarring which follows the treatment with fuming nitric acid? To my mind, the only treatment necessary for dog bite is the usual treatment given in any other wound which might be infected, plus the Pasteur treatment if the dog is rabid or if there is a suspicion that the dog is rabid. It seems to me that there is a lot of unnecessary disturbance about the treatment of the usual dog bite.

MARVIN D. SHIE, M.D., Lakewood, Ohio.

ANSWER.—There is certainly a difference of opinion on this subject and there is some weight to the view expressed. Some believe that there is no logical basis for the assumption that the use of fuming nitric acid prevents the development of rabies. Others, as previously mentioned, maintain that nitric acid should be used if the dog is mad, has suggestive symptoms or is unidentified. Experiments with guinea pigs seem to show that rabies can be prevented in a large number by means of fuming nitric acid. In the light of present available evidence it does not seem that one should be criticized for the use of nitric acid, although in a few years the entire method of treatment may be changed.

## BENZOYL PEROXIDE IN FLOUR

*To the Editor:*—Please give me some information concerning the toxicity of benzoyl peroxide, sold under the trade name of Novadel and used as a bleaching agent in the preparation of flour. I understand that this substance is used in the proportion of 1 ounce to 200 pounds of flour. What harmful effects, if any, might be expected from ingestion of flour in which this substance was used in the proportion of 50 ounces to 200 pounds?

M.D., Oklahoma.

ANSWER.—The usual person consumes less than 1 pound of flour a day, but an exceptionally active man, consuming in the neighborhood of from 4,000 to 5,000 calories daily, may utilize as much as 2 pounds in the form of bread, pastry and sauces. Under these extreme conditions, such a person might consume one-half ounce of the benzoyl peroxide if flours containing the peroxide in the proportions of 50 ounces to 200 pounds were ingested. In toxicology, this substance is chiefly associated with bakers as one of the sources, but perhaps not the foremost source, of "bakers' itch." The substance enjoyed some use as an external disinfectant and skin anesthetic but occupies a position today of little recognition. Little is known about its action after ingestion in large quantities, but there are reasons to believe that it may cause gastrointestinal irritation and hamper digestive processes through local anesthetic action. In the intestinal tract it is believed to decompose in part to benzoic acid and/or benzaldehyde.

Paul D. Lamson (THE JOURNAL, Aug. 30, 1930, p. 663) states that benzoyl peroxide "is extremely nonirritating, watery solutions causing no irritation when dropped in the eye, and even the pure crystalline substance causing no irritation or disturbance of any kind when placed in the peritoneal cavity. It is also nontoxic when taken by mouth, being reduced to benzoic acid and excreted as hippuric acid. Saturated water solutions have been given intravenously without toxic effects."

Note is made of the fire and explosion hazard related to this substance. Reports of accidents with benzoyl peroxide are on record, and caution should be exercised in handling it.

It should be further noted that the proportion of 50 ounces of benzoyl peroxide to 200 pounds of flour, or one part of benzoyl peroxide to sixty-four parts of flour, appears excessive. The Council on Foods has accepted a number of brands of flour which are artificially bleached with nitrogen chloride and a mixture of calcium phosphate and benzoyl peroxide in the proportions of one-tenth ounce of nitrogen chloride to 196 pounds of flour and one part of the mixture of calcium phosphate and benzoyl peroxide to 50,000 parts of flour. Two pounds of such flour would contain a maximum of 0.02 Gm. of benzoyl peroxide. Available evidence (Sollmann, Torald: A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1936, p. 602) indicates that healthy persons may safely consume as much as 0.5 Gm. of benzoate a day in concentration of 0.1 per cent if these foods are not otherwise spoiled or unhealthful but that patients with gastrointestinal diseases would do better to avoid it. It is quite conceivable that irritant actions which would be too feeble to influence normal organs might become deleterious to these organs, especially the gastrointestinal tract or kidneys, if these are already diseased or if the general resistance is lowered. The Council on Foods requires that all accepted flours which are artificially bleached carry the word "Bleached" in a conspicuous position on the package label and publishes with each announcement of acceptance the amount and kind of bleaching agent used.

## CONTACT DERMATITIS FROM RHODIUM OR NICKEL

*To the Editor:*—A woman acquired a local contact dermatitis from wearing a bracelet for several hours. The bracelet consisted of a basic white metal on which had been successively plated nickel and rhodium. Could the rhodium, which was the superficial metal, have been the cause of the dermatosis? If so, what is the relationship to skin hypersensitiveness? What are the other possibilities?

M.D., New York.

ANSWER.—The diagnosis of contact dermatitis in this case is obvious. The only question is as to the cause, whether nickel or rhodium or perhaps some other metal. Rhodium is a metal in the platinum group and is closely allied to iridium. It is used in the manufacture of liquid gold and is also used as an outer coat in some silverware to prevent tarnish. Some of the salts of rhodium are pink, and some cosmetics may possibly contain one of these salts, although this has not been proved.

A search of the literature revealed no reports of dermatitis due to rhodium. On the other hand there have been many cases of dermatitis from contact to nickel. Weber (External Causes of Dermatitis, *Arch. Dermat. & Syph.* **33**:129 [Jan.] 1937) gives a list of external irritants and a review of the literature on contact dermatitis. Foster and Ball (Sources of Nickel Eczema, *ibid.* **31**:461 [April] 1935) review the literature on nickel dermatitis and report several cases. They consider nickel capable of causing a definite sensitivity; they state that the incubation period is from eight to thirty days between the first contact with nickel and the development of the dermatitis.

To discover the cause in this patient, patch tests with nickel and rhodium should be made on clear skin, e. g. the back. Foster and Ball give the details. The test is simple.

Contact dermatitis is a form of hypersensitiveness in which the skin alone suffers. Almost every one can acquire contact dermatitis provided the contact is sufficiently close and sufficiently prolonged. This has been proved in cases of primrose sensitivity, which is another variety of contact dermatitis. Patch tests are usually positive and ordinary cutaneous and intracutaneous tests are negative. There is no family history of allergy and passive transfer tests are negative. In one of the "nickel" cases of Foster and Ball the passive transfer test was reported as positive.

## WAX FOR REMOVAL OF HAIR—X-RAYS AS DEPILATORY

*To the Editor:*—1. Please furnish a prescription for preparing a wax which may be applied to the body and by its removal extract excessive hair. How is it used? How often would a heavy growth of black hair have to be removed from the legs with wax? Is there a better method of meeting the situation than by removal with wax? 2. Is there a safe method of removing an excessive growth of hair from the eyebrows and forehead by means of x-ray treatments?

M.D., California.

ANSWER.—1. The simplest formula for epilating wax is that given by William Allen Pusey (Recipe for Epilating Wax, THE JOURNAL, Aug. 28, 1926, p. 663): beeswax 1 part by weight, finely powdered rosin 4 parts by weight. Melt the beeswax over a slow fire and pour in the rosin, stirring gently for a few minutes until all is melted. Mold on a greased dish, marking the cooling cake in rectangles, or pour into cylinders of waxed or greased paper with the bottom folded shut.

There are a number of more complicated formulas. There is no reason to think that they are any better than the simplest.

To apply, heat one of the cakes on the end of a stick over a flame until soft. When cooled to a bearable temperature, rub it on the hair to be removed, rubbing in the direction of the hair, until the wax is about an eighth of an inch thick, pressing it down well on the hair. When cool, loosen the end next the ends of the hair and pull off the whole mass in the direction

opposite to the growth of hair. If well done only a few hairs will remain and these can be removed with tweezers. Pusey states that the procedure is only slightly uncomfortable.

The advantage of this method lies in its applicability to a generous growth of fine hair, a difficult, tedious and expensive task for electrolysis. The result is much more lasting than that from shaving or chemical epilation. It is impossible to say just how quickly the hair will return after this procedure. It depends on the individual and the part of the skin involved; but another treatment should not be necessary for at least two months, according to Giovannini, quoted by Jackson and McMurtry (Diseases of the Hair, Philadelphia, Lea & Febiger, 1912, p. 42).

The other practical methods of hair removal are by electrolysis, shaving and chemical depilatories, the latter of which must be repeated frequently, and grinding down the hair by rubbing with pumice stone in powder or cake form. The latter has its advocates, who claim that continued use of it reduces the hair growth. The method is tedious and it requires some experience to acquire the proper technic. If the hair is coarse, it should be cut short before beginning and it is claimed that lathering the skin makes for success. After the first grind, which may take a half hour to remove the hair completely, it is claimed that a few minutes rubbing each day will keep down the growth and that this can be done without serious skin irritation.

2. An emphatic negative must be returned. Any strength of roentgen rays sufficient to cause atrophy of the hair roots is sure to result in visible atrophy of the skin sooner or later, often with disfiguring telangiectasis. This may not appear for years after the original injury.

## RHEUMATOID ARTHRITIS OF SPINE?

*To the Editor:*—A college graduate, aged 21, weighing 154 pounds (70 Kg.), complains of pains in the adductor muscles and knees and in the lumbosacral region, and of inability to lie quietly for more than three or four hours because of pain. He has had scarlet fever, measles, pertussis and bronchitis during childhood, all of which he recovered from with no complications. In 1933 he had Vincent's angina, in 1934 gonorrhea, for which he has taken treatments regularly for two years, and repeated prostatic smears which have been examined in reliable laboratories and have not shown the presence of gonococcic infection. In 1936 while at college he was hospitalized for influenza. About four months ago he began to complain of pains in his knees, adductor muscles of his legs and in his back, which have been continuous since. There has not been any swelling or redness of the knees or of the involved muscles. The pain bothers him severely after lying in bed about three or four hours and he awakens at about 4 in the morning with severe backaches, which are relieved by moving about. These backaches are worse if he has exercised strenuously the previous day but at the time of exercise he does not feel worse. The pain in the adductor muscles of the legs radiates into the scrotum and these muscles are also painful on coughing. There is no increase in pain during sexual relations. Examination showed a white blood count of 13,000, temperature of 99.2 F. and a pulse rate of 96. The blood pressure is 120 systolic, 80 diastolic. The urine is negative for pus, albumin, sugar and blood cells; the sedimentation rate is within the normal range after one and three hours. The tonsils and teeth show no signs of infection. There are no glandular enlargements. Heart and lung examinations are negative; the abdomen is normal. The prostate was normal to palpation and the secretion contains only a few pus cells. The involved regions of the back, legs, scrotum and knees show no evidence of inflammation or edema and are not tender. While at school the patient was told by one doctor that it was not his previous gonorrhea causing his trouble and advised him to have his tonsils removed. Another told him that since his tonsils showed no infection this would be illogical. I agree with this. His condition was diagnosed as neuritis by the second doctor, who treated him with diathermy, a vitamin B compound, rest and the use of a hard, flat bed. He has now returned home for the summer and during the last three weeks has been getting worse. It appears that the man has an infection but I am at a loss to say where. I have also done an agglutination test for Malta fever, which was negative.

M.D., South Dakota.

ANSWER.—It is impossible to make an absolute diagnosis from the data presented. From the information at hand, one should be suspicious of a beginning rheumatoid arthritis involving the spine (Marie-Strümpell type of spondylitis). This diagnosis would adequately explain the low grade fever, leukocytosis, all the symptoms, and the otherwise negative physical examination. X-ray examination of the sacro-iliac joints may reveal bilateral sacro-iliac arthritis. If this is found, the suspicion will be corroborated. One occasionally sees a case of rheumatoid arthritis in the early stages with a normal sedimentation rate. In this particular case a sedimentation rate done by the Rourke-Ernstene method might reveal an abnormal rate. A differential blood count might show a shift to the left. It is improbable that the previous gonorrheal infection has any part in the present illness, nor is it likely that the removal of the tonsils would materially benefit the patient.

If he has a beginning Marie-Strümpell spondylitis, physical examination might reveal limited chest expansion, pain at times on deep breathing, spasm of the psoas muscles or the paravertebral muscles, tenderness over either sacro-iliac joint and limited straight leg raising. If the fever and leukocytosis do not persist, one should examine the patient for other causes of backache, such as a ruptured intervertebral disk, lumbosacral strain, postural strain, cord tumor and the like. A complete neurologic examination and detailed examination of the skeletal system should help to make a diagnosis.

If subsequent studies reveal that the patient is suffering from rheumatoid arthritis of the spine, the treatment indicated would be adequate bed rest, a high vitamin, high caloric diet, hot fomentations to the back, control of pain, sleeping on a firm bed, exercises, vitamin concentrates if indicated and a sacro-iliac belt for support if needed.

## COMPOSITION OF PATHOLOGIC CALCIFICATION

*To the Editor:*—Can you tell me the chemical composition of the deposits found in calcified subdeltoid bursitis? I have not been able to find any chemical analysis of this material in any of the articles to which I have had access and would appreciate knowing in just what form this calcium is deposited.

M. E. GOODRICH, M.D., Toledo, Ohio.

ANSWER.—The composition of deposits of pathologic calcification has been studied by MacCordick, Wells and Codman.

H. Gideon Wells (Chemical Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1925, p. 487) concluded that the chemical composition of deposits in the various types of pathologic calcification was essentially the same as that of bone. Dr. A. Baird Hastings made chemical analyses of the deposits found in calcification of the supraspinatus tendon and subdeltoid bursae and concluded that the composition was essentially the same as that of bone ash. (This work has not been published.)

E. A. Codman (The Shoulder, Boston, Thomas Todd Company, 1934, p. 79) has published the most complete studies of the composition of these deposits. The chemical analyses were made by Dr. J. L. Stoddard, who found that deposits of the inorganic matter of the dried unashed specimen contained 55.8 per cent of calcium phosphate and 42.2 per cent of calcium oxalate. There was 14 per cent of the ash that could not be accounted for by figuring all the phosphate as calcium phosphate and the remaining calcium as carbonate. What this 14 per cent consisted of was not definitely established.

## NICOTINE POISONING AND SPRAYING HAZARDS

*To the Editor:*—What is the health hazard arising in an unmasked person from spraying the following solutions in a greenhouse? The sprayer is exposed for periods of from eight to ten hours daily and no protective measures are employed. The greenhouse contains principally flowers with a high humidity and temperature present. 1. Aqueous solution of 40 per cent nicotine. 2. "Selocide," a commercial product containing 8 per cent potassium ammonium sulfide and seleno sulfide. Any information you can give me on this subject will be appreciated.

R. D. HOWELL, M.D., Indianapolis.

ANSWER.—While various greenhouse plants may lead to dermatoses from direct irritation or as a result of sensitization, and while selenium compounds, as mentioned in the query, and other insecticides may possess some toxic properties, nicotine must be regarded as highly and practically dangerous. Toxicologic literature contains many references to fatalities and to severe poisoning connected with exposure to insecticides containing nicotine. A typical occurrence, appearing in the literature is here excerpted: A girl, employed in the manufacture of insecticides, spilled a few cubic centimeters of a 95 per cent solution of nicotine (probably in the form of sulfate) on one sleeve. Promptly she washed and dried her arm, wiped it on undersleeve and changed her overalls. Twenty minutes later she collapsed and became pallid and cold, and the pulse was not perceptible. Nicotine was established as present in the vomitus. This patient recovered. This article (*Brit. M. J.* 1:246 [Feb. 11] 1933) carries the statement "Clearly nicotine is a powerful poison when applied to the skin, from which it should be removed by washing with cold water instead of hot, which by flushing the skin increases the rate of absorption." This statement may be supplemented by noting that nicotine poisoning may be induced following either inhalation or ingestion. The lowest grade of nicotine poisoning may be accompanied by dizziness, headache, nausea and vomiting. A slightly severer state in addition may include clammy sweating, visual disturbances, profuse ptyalism, diarrhea and collapse. When nicotine is ingested, a sensation of burning may exist in the mouth, gullet and stomach. In severe poisoning, when death does not take place in a few seconds or minutes, mental confusion may appear, together with muscular weakness, restlessness, quick and labored respiration, feeble and irregular heart beat, convulsions and

muscular twitchings. In view of the extensive and often careless use of nicotine insecticides, it appears likely that some degree of tolerance may develop, as in the case of tobacco smokers.

The possibility of selenium poisoning exists, but the nature of selenium poisoning and the conditions under which it arises are not well known. More information may be found in "Studies on the State of Selenium in the Organism," by M. I. Smith, B. B. Westfall and E. F. Stohlman (*Pub. Health Rep.* **53**:1199 [July 5] 1938). It is to be noted that nicotine readily harms rubber, so that natural rubber gloves or gauntlets are somewhat unpractical, but some types of synthetic rubber are more resistant to nicotine action. In the presence of a definite nicotine exposure, as implied in the query, other mentioned exposures, as high humidity and temperature, may be ignored as relatively unimportant.

## NEUROCIRCULATORY ASTHENIA

*To the Editor:*—Physical examination of a man aged 43 reveals the following: bright, 5 feet 6½ inches (168 cm.); weight, 165 pounds (75 Kg.); pulse rate, 94 (next day 114), usually from 90 to 100; respiratory rate, 22; temperature, 98.6 F.; blood pressure, 100 systolic, 80 diastolic (always around 100); hemoglobin, 74 per cent; white cells, 11,900; red cells, 5,150,000; urine, normal; basal metabolism, plus five per cent; Mantoux test, negative; Wassermann reaction, negative; eyegrounds, normal. While blood was being drawn for a Wassermann test he had a distinct convulsion of some sort. Convulsive movements of the arms and legs occurred, the eyes rolled back and he lost consciousness for two or three minutes. Immediately after this seizure his pulse was normal for a short time: within a period of ten minutes it dropped from 100 to 72 and remained that way until he left my office a short time afterward. He is the picture of health. He came to me because of terrible attacks of depression. He has these attacks without any cause whatever and they have lasted several weeks at a time. Instead of going to his office he remains around his home and is not fit to do any work. He is secretary and treasurer of a corporation, a position which requires much bookkeeping. He is in good circumstances financially. He tells me that he has nothing to worry about at all but that he gets these attacks just the same. X-ray examination of the chest gives negative results. The low blood pressure and constantly rapid heart make me think of Addison's disease but it is not a clear picture of anything that I know of. What can I do for him?

M.D., Indiana.

ANSWER.—The condition which seems most probable is an "autonomic imbalance" or "neurocirculatory asthenia." These terms are really a cloak for ignorance of the actual underlying cause for a clinical syndrome. It is assumed to be some sort of maladjustment between the sympathetic and parasympathetic systems. It is associated with tachycardia, easy fatigue, low blood pressure, syncopal attacks and a general feeling of inadequacy leading to mental depression. It is assumed that the convulsive seizure was a syncopal attack. The one important requirement for diagnosis is that all organic pathologic changes be ruled out. It would not appear that a moderately low blood pressure makes an adequate basis for a diagnosis of Addison's disease.

One must also consider as possibilities a neurosis or a psychosis. An anxiety neurosis or a mild depressive psychosis will present a picture resembling this one. The differential diagnosis of these conditions may be found in any standard textbook on neurology and psychiatry.

The treatment of a neurosis or a psychosis is a highly specialized problem. The treatment of neurocirculatory asthenia is one of intelligent management and encouragement and the avoidance of drugs. Any further suggestions for treatment must be based on a more accurate diagnosis.

## CHORDOTOMY FOR SCIATIC NEURALGIA

*To the Editor:*—A chordotomy has been proposed for a patient with severe and protracted sciatic neuralgia presumably due to osteo-arthritis of the spine. Can you give me any information as to the dangers and permanent value of such an operation in the hands of a skilful neurosurgeon? What about the operation of rhizotomy of the posterior nerve roots?

A. T. BLACHLY, M.D., Portland, Ore.

ANSWER.—Either operation suggested appears drastic, but it is assumed that the case is one of unusual severity and long duration and that both sides are affected. Section of the posterior roots is of such uncertain value that it may be dismissed. Bilateral chordotomy in the thoracic region is reasonably certain to give great relief. However, even the most experienced and dexterous neurosurgeon may cut too much, causing some paralysis, or too little, in which case little or no relief is secured and the operation would have to be repeated to be of benefit. However, if all usual methods of treatment have failed chordotomy is the last resort, but the risks should be explained to the patient.

## DIAGNOSIS OF SYPHILIS?

*To the Editor:*—A white woman aged 33 reports that in 1927 a Wassermann test showed a strongly positive reaction. A second Wassermann test was then taken and reported negative. She was told to disregard the first report and received no treatment. About a year later she missed her menstrual period and consulted an obstetrician, who told her she was pregnant. A Wassermann test taken at this time was returned four plus. She received one injection of neoarsphenamine, and another Wassermann test taken about a week after the first was negative. She received no further treatment, but several Wassermann tests taken during her pregnancy were all negative. She delivered a normal full term baby whose Wassermann reaction was negative. Her husband's Wassermann test, taken shortly after hers was returned positive, was negative. She has remained fairly well since the baby was born but has had three spontaneous abortions, all within the first three months of pregnancy. One year ago she had a hemorrhoidectomy because of bright red blood in the stools, pain on defecation and a feeling of fulness in the rectum and of aching in her back and hips. Following the hemorrhoidectomy the rectum was sore for three or four months and the bleeding has continued until the present time. She says that her rectal condition has not been altered in the least by her operation. At the present time she feels nervous and is easily excited and irritated, in addition to her rectal complaint of bleeding, fulness and discomfort on bowel movement, and aching in the hips and back. Her only past illness was diagnosed as scarlet fever at the age of 20. She was not acutely ill and does not remember having peeled at all. There has never been sexual intercourse with any one except her husband. Physical examination at present is negative except for a presystolic mitral murmur, stellate laceration of the cervix, many tags about the rectum and moderately sized internal hemorrhoids. X-ray examination of the chest reveals normal heart and lungs; the blood count and urinalysis are normal. Kolmer's Wassermann reaction was 4 plus in three tubes, twenty-four hours later 2 plus, 2 plus and 1 plus, and twenty-four hours later was reported negative by two competent laboratories. Her spinal fluid was entirely normal. I shall appreciate discussion of the status of this patient.

M.D., Texas.

ANSWER.—It is difficult to say whether this patient has syphilis or not. Much depends on who did the Wassermann test and the type of reaction. It is known that there are such things as false positive Wassermann reactions. At the recent meeting of the American Medical Association in San Francisco there was considerable discussion in the Section on Dermatology and Syphilology on certain cases that have been carefully studied by syphilologists and the blood checked in many different first class laboratories with confusing reports. Another Wassermann test should be taken on the baby, for it is known that a child may have a negative Wassermann reaction at birth and later the serologic reaction may change. The patient's rectal difficulty is apparently from hemorrhoids and can in no way be attributed to syphilis. Moreover, there may be some other explanation for the three spontaneous abortions, for this does not necessarily mean syphilis. As the patient's physical examination is negative, her spinal fluid is entirely normal and she still has what one might term a controversial serologic report on her blood, one would be inclined to recommend no treatment for syphilis. It would probably be well, however, to examine her carefully each year. It might even be advisable to have consultation with a competent internist or syphilologist.

## INTERMITTENT HYDRARTHROSIS

*To the Editor:*—A white man aged 76, with mild diabetes, has recurring simple nontraumatic hydrarthrosis of the left knee joint of about one year's duration. During the year the knee has been aspirated about six times. Culture of the fluid was negative. Twice the knee was immobilized with a cast for about ten days and then treated with diathermy and strapping. The patient has little pain and enjoys good health. He had a prostatectomy about six years ago and the urine is still cloudy. Can you suggest any other treatment, such as injection of air or other medication? Please describe technic.

M.D., New York.

ANSWER.—Two types of intermittent hydrarthrosis are recognized: the first and rarer type is "true intermittent hydrarthrosis," which usually involves one or both knees in recurring attacks remarkable for their regularity, attacks generally coming every ten to fifteen days and usually lasting from two to six days. The second type, "symptomatic intermittent hydrarthrosis," is commoner and represents the early stage of chronic synovitis or of atrophic arthritis which has not yet become generalized but of which, for a while, the symptoms are confined intermittently to one joint, later becoming chronic and polyarticular. If, after one year, this patient presents no evidence of polyarticular involvement and if the erythrocyte sedimentation rate, nonfilamented cell count and erythrocyte count are normal, he may have the first type. To distinguish the two conditions more accurately and promptly, further studies on the comparative cytology and chemistry of synovial fluid are needed. In true intermittent hydrarthrosis the total synovial fluid cell count is generally low (from 400 to 7,000 cells per

cubic millimeter); in atrophic arthritis it is generally considerably higher (from 5,000 to 60,000 cells per cubic millimeter).

The cause of true intermittent hydrarthrosis is unknown. Because the effusions appear rapidly and periodically and disappear without leaving a symptomatic residue, the disease is thought by some to be due to angioneurosis; hence the allergic hypothesis has been advanced. It remains unproved, however. Endocrine disturbance or infection is believed responsible by others. Several cases of intermittent hydrarthrosis associated with undulant fever have been reported (Baker 1928, 1929; Simmons 1935; Sharpe 1936).

Many forms of treatment have been advocated: removal of foci of infection, desensitization by injections of peptone, intravenous injections of triple typhoid vaccine, arsenic, rest, physical therapy, bandages, splints. Ergotamine tartrate (gynergen) was considered of value by Weismann-Nutter (1929). Sometimes the cycles are interrupted temporarily or permanently after the use of one or more of these various measures; in other cases the cycles persist. The hydrops often ceases spontaneously after some months or years. When it seriously handicaps the patient's health or earning power, synovectomy may be indicated (Porter and Lonergan 1932; Krida 1933).

## CORD BLADDER AND IMPOTENCE AFTER DISSEMINATED MYELITIS

*To the Editor:*—A man aged 21 reports that five years ago he had what was diagnosed as acute disseminated myelitis. He was paralyzed from the nipples down but recovered by March 1934. All muscular reactions are normal as well as touch sensation, but he is having trouble with poor bladder control and constipation is extreme. It is impossible for him to have an erection and he has no natural desire for intercourse. As he wants to get married, he would like to know if there is any possibility of improvement along this line.

M.D., Illinois.

ANSWER.—One would expect to find on a sensory examination some disturbance in the sacral region, i. e. saddle anesthesia. Disturbances in urination, defecation and erection indicate a lesion of sacral levels 2, 3, 4 and 5, which is probably a residue of the disseminated myelitis. Cystoscopic examination would probably confirm the diagnosis of cord bladder.

The prognosis depends on the extent of the lesion and whether a normal libido was present and intercourse was possible before the attack. Cases have been described in which erection and intercourse were perfectly possible in extensive lesions of the sacral cord. This is probably due to a cerebral (psychic) mechanism, although bladder and rectal disturbances were still present.

One should try drugs such as strychnine to stimulate any nerves present (1 mg. four times a day). Ergotamine tartrate (gynergen) has been used in tabetic bladders with fair results and may be of some value here. As a last resort some of the androgens should be injected parenterally to see whether some sexual desire could be initiated.

The prognosis at its best is not too favorable but these measures should be tried.

## ALLERGY TO CHLORINE

*To the Editor:*—A youth aged 17 apparently has an allergy to chlorine in bath water, as he breaks out in large red welts during or immediately after a bath. During two years in Virginia, where the water supply is artesian and not chlorinated, this did not occur, but on his return to Chicago it is again manifest. Every type of soap, and no soap, have been tried, but the result is the same. Can you suggest a remedy? His older brother, aged 32, is affected much the same way but less severely. While driving across the Appalachian Mountains five years ago, the same boy complained of pain in his ears on descending from an altitude of 3,000 feet. This sensitiveness has continued through several similar trips and now he feels it when descending in an elevator. Is there any remedy?

M.D., Illinois.

ANSWER.—Allergy to chlorine, while not definitely accepted, has been reported. Duke (*J. Allergy* **3**:495 [July] 1932) had a patient, a physician, who acquired coryza, cough and asthma from the use of Dakin's solution, and to the chlorine gas which escaped from diluted solution of sodium hypochlorite. Chlorinated water caused wheals in this patient. Passive transfer of this hypersensitivity to chlorine was not successful. Duke believes that this type of allergy is similar to that found in physical allergy.

Watson and Kibler (*ibid.* **5**:197 [Jan.] 1934) reported a case in which chlorine in drinking water was apparently the cause of asthma and colitis. The patient became worse when drinking chlorinated water and was entirely relieved on changing to distilled water. In the discussion which followed the presentation of this paper, Eyermann stated that he had relieved two patients of intractable urticaria by the use of distilled water. These patients had failed to respond to ordinary elimination diets. Milton Cohen discussed the case of a chemist who had coryza from the inhalation of platinum chloride.

Dutton (*ibid.* **6**:477 [July] 1935) reported a case in which severe eczema resulted from the drinking of ordinary tap water; when distilled water was substituted on numerous occasions, the eczema cleared up quickly each time. The author concluded that some allergen or other substance in the drinking water was the etiologic factor but did not specify what this substance was.

From these reports it seems evident that the patient under consideration must avoid contact with chlorinated water. Apparently contact with the water is sufficient. If there is a possibility that drinking such water causes the urticaria, distilled water should be substituted.

The simplest remedy for the pain in the ears on descending from high altitudes is to stuff cotton in the ears.

## DERMATITIS FROM BATHING SUIT DYE

*To the Editor:*—I am reporting a case of pigmentation of the thigh following the running of a red dye from a bathing suit. The patient exposed herself to the sun, and some photosensitizing dye in the bathing suit produced this pigmentation. In reviewing the literature I have been unable to find a case of pigmentation from a photosensitizing dye. Would you please inform me whether such a case has been reported and also name the several red dyes which might have been used in dyeing this bathing suit? The pigmentation is similar to a "berloque" dermatitis.

I. LEWIS SANDLER, M.D., Washington, D. C.

ANSWER.—From the description, the case mentioned could well fit into the broad classification of "berloque" dermatitis. No report of such a case has been found, but the red dyes used in bathing suit manufacture fall within the eosin group, and it is conceivable that the eosins and erythrocein group have photosensitizing properties. For further technical information, consult Occupational Affections of the Skin by R. Prosser White (New York, Paul B. Hoeber, Inc.).

## TRAUMATIC APPENDICITIS

*To the Editor:*—Further in regard to the report of Dr. Donald B. Rogers (THE JOURNAL, September 24, p. 1231) in reply to Dr. Royal H. Fowler (THE JOURNAL, July 30), I wish to mention the following case:

A WPA worker aged 37, giving no previous history of a disorder of the gastrointestinal tract, slipped and fell on a sewer main pipe with the weight and impact of the pipe he had been lifting coming down on his abdomen. He had been lifting this pipe, which weighs about 300 pounds, with four other men, and as he slipped their hold gave way and the patient's abdomen became wedged in between the rims of the heavy mains. This happened just before quitting time on a Saturday noon. He immediately felt a twinge in his side. He was able to reach home and vomited an hour after the injury. Pain became worse and for relief he took a little ginger and peppermint, thinking it was indigestion. That same night he vomited twice and on Sunday six times, with no relief of pain in the lower right quadrant of the abdomen. On this second day the patient seemed markedly ill; clinical and laboratory examinations pointed to a ruptured appendix. Operation confirmed this, showing a ruptured retrocecal appendix with spreading peritonitis. Recovery followed a stormy convalescence.

I ascribed this case to trauma, direct traumatic injury to the appendix with infection immediately superimposed at the site. I do not believe that a previous infection in the appendix is necessary to traumatic appendicitis but that the infection is carried on an injured area shortly after the injury. I do not believe that, as a requisite to diagnosis of traumatic appendicitis, the presence of previous disease, which would mean chronic appendicitis, is necessary, as upheld by the industrial commissions.

The WPA compensation commission in Washington holds that there is no such entity as traumatic appendicitis, giving this reason for ruling against this case. It sits in its cases, at least, as the final seat of judgment and establishes that there is no traumatic appendicitis.

EMIL S. GOODYEAR, M.D., Kingston, N. Y.

## SPASMS OF LEGS AT NIGHT

*To the Editor:*—The reply given on page 2103 of the June 18 issue of THE JOURNAL to the physician who inquires about spasms of the legs at night seems somewhat incomplete. Nocturnal muscle cramps frequently occur in person beyond middle age and are not related to any form of peripheral vascular disease. Typical attacks occur in persons whose peripheral circulation is entirely normal. The cramps can be relieved in dramatic fashion by the administration of small doses of calcium lactate. In my experience with about thirty such cases 5 grains (0.3 Gm.) of calcium lactate an hour before meals has invariably relieved the symptoms. It is reported that from ten to fifteen drops of diluted hydrochloric acid in water with each meal will also act promptly in a similar manner. The following references will be of interest to the physician who inquired in regard to this condition:

Steven, R. A.: Muscle Cramps During Sleep, THE JOURNAL, Nov. 10, 1934, p. 1475.

Mills, C. A.: Muscle Cramps During Sleep, THE JOURNAL, Sept. 29, 1934, p. 1015.

SAMUEL SILBERT, M.D., New York.

# Medical Examinations and Licensure

## COMING EXAMINATIONS

### STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, October 29, page 1685.

### SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral*, St. Louis, Nov. 11-12. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 13-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., January. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Rochester, N. Y., November 13 and Oklahoma City, November 15. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15 Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

## Nebraska June Examination

Mrs. Clark Perkins, director, Bureau of Examining Boards, reports the written examination held at Omaha, June 8-9, 1938. An average of 75 per cent was required to pass. Eighty-one candidates were examined, all of whom passed. The following schools were represented:

| School | PASSED | Year Grad. | Number Passed |
|---|---|---|---|
| Northwestern University Medical School | (1933), | (1938) | 2 |
| University of Louisville School of Medicine | | (1936) | 1 |
| Creighton University School of Medicine | (1938, 13) | | 13 |
| University of Nebraska College of Medicine | (1936), (1937, 2), (1938, 62) | | 65 |

Four physicians were licensed by reciprocity from March 16 through July 26. The following schools were represented:

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| State University of Iowa College of Medicine | (1936), | (1937) | Iowa |
| University of Michigan Medical School | | (1928) | Michigan |
| New York Homeopathic Medical College and Flower Hospital | | (1909) | New York |

## Ohio Reciprocity and Endorsement Report

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports forty-two physicians licensed by reciprocity and five physicians licensed by endorsement July 19, 1938. The following schools were represented:

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| Loyola University School of Medicine | | (1936) | California |
| Rush Medical College | | (1919) | Michigan |
| (1936) West Virginia, (1936), (1937) Illinois | | | |
| Indiana University School of Medicine | | (1933) | Indiana |
| State University of Iowa College of Medicine | (1934), | (1937) | Iowa |
| University of Kansas School of Medicine | | (1937) | Kansas |
| University of Louisville School of Medicine | (1935), (1936), (1937) Kentucky | (1925), | |
| Johns Hopkins University School of Medicine | (1933), | (1935) | Maryland |
| University of Michigan Medical School | (1937) Michigan | (1931), | (1936), |
| Wayne University College of Medicine | | (1938, 2) | Michigan |
| St. Louis University School of Medicine | | (1937, 4) | Missouri |
| Washington University School of Medicine | | (1934) | Missouri |
| University of Nebraska College of Medicine | | (1935) | Nebraska |
| University of Buffalo School of Medicine | | (1937) | New York |
| Temple University School of Medicine | | (1936, 2) | Penna. |
| University of Pennsylvania School of Medicine | | (1933) | Penna. |
| University of Pittsburgh School of Medicine | (1934), (1935) Pennsylvania | (1932), | |
| Meharry Medical College | | (1935) | Louisiana, |
| (1931), (1934), (1936) Tennessee | | | |
| University of Tennessee College of Medicine | | (1937) | Tennessee |
| Vanderbilt University School of Medicine | | (1932), (1937) | Tennessee |
| University of Alberta Faculty of Medicine | | (1929) | New York |
| Universität Bern Medizinische Fakultät | | (1935) | Maryland |

| School | LICENSED BY ENDORSEMENT | Year Endorsement Grad. | of |
|---|---|---|---|
| Yale University School of Medicine | (1934), | (1935) | N. B. M. Ex. |
| Harvard University Medical School | | (1934) | N. B. M. Ex. |
| Tufts College Medical School | | (1933) | N. B. M. Ex. |
| Duke University School of Medicine | | (1935) | N. B. M. Ex. |

# Book Notices

**A Manual on Pharmaceutical Law Together with Appendices Containing Important Laws of Congress, the Uniform Narcotic Drug Law, and Other Laws Relating to Pharmacy.** By C. Leonard O'Connell, Dean of the Pittsburgh College of Pharmacy, University of Pittsburgh, Pittsburgh, and William Pettit, Member of the Pittsburgh Bar. Cloth. Price, $2.50. Pp. 198. Philadelphia: Lea & Febiger, 1938.

Few fields, the authors say, have as frequent and daily contact with rules and regulations as the profession of pharmacy; and he certainly proves his case, as may be seen from the chapter headings, which cover government and the regulation of pharmacy, state regulation, federal regulation, the pharmacist's liability for negligent acts, the pharmacist's liability for negligence of the employee, other rights and liabilities, contracts relating to the sale of drugs, bankruptcy, insurance and trade restraints. There is an appendix dealing with the Harrison Narcotic Law, the federal Food and Drugs Act, the federal criminal law relating to nonmailable matter, and other important laws. In chapter I the author explains that the federal government, in respect to delegated powers, is supreme but that it is restricted to a far greater extent than the state governments, which in the exercise of their "police power" may variously regulate the practice of pharmacy and the sale of drugs and poisons. To the physician the question of the ownership of prescriptions is of special interest: a question not definitely decided by the courts. Reading between the lines, it is obvious that the customer owns the prescription until it is filled, then the pharmacist shall keep the prescription on file for a period of years, usually five. For such a period, at least, the customer cannot demand return of his prescription. No decision is available as to whom the prescription belongs after the lapse of the five years, but common sense should dictate that at the end of this time the pharmacist may destroy the prescription if it is not called for at that time. Pharmacists are prohibited from practicing medicine, but that means they are really merely prohibited from making diagnoses and from an actual application of remedies. The pharmacist in instructing as to the use of a medicine after he has sold it would not be diagnosing or treating disease.

**Nouvelle pratique dermatologique.** Publiée par MM. Darier, Sabouraud, Gougerot, Millian, Pautrier, Ravaut, Bézary, Clément Simon. Secrétaire général, Clément Simon. Tome VII: Maladies des annexes de la peau. Dermatoses non classées. Dermatologie comparée. Par MM. Ch. Audry et al. Boards. Price, 300 francs. Pp. 894, with 407 illustrations. Paris: Masson & Cie, 1938.

The first 240 pages of volume VII are the contributions of Sabouraud alone and in collaboration with Pignot on the hair and sebaceous glands. There is so much disagreement among dermatologists as to what constitutes pityriasis simplex, pityriasis steatoides and the seborrheic states that every one should take advantage of the opportunity of reading this clear and logical presentation of the subject. According to Sabouraud, pityriasis of the scalp is an exfoliation of the corneous layer of the skin due to the Pityrosporon of Malassez. The two photomicrographs on pages 28 and 29 showing the similarity between sections of pityriasis simplex and pityriasis versicolor are convincing. Most of the textbooks describe seborrheic dermatitis as beginning in the scalp and spreading down over the face. Sabouraud reverses the sequence of events and insists that the seborrhea begins on the face and spreads to the scalp. The apparently oily masses formed in pityriasis steatoides are not only not greasy but contain less oil than is found in normal exfoliation of the corneous layer. "The patient is aware that his scalp quickly becomes dirty and that when he scratches it with his nails he removes dirt which has a greasy appearance and

which most dermatologists consider to be glandular secretion, in other words seborrhea, but which as a matter of fact is a surface exfoliation infiltrated by serum exuded from the surface of the epidermis. Such a state is accompanied by a loss of a few hairs but in slight proportion. There is very little alopecia even with pityriasis steatoides. The alopecia is really seborrheic, that is to say in connection with the infection by the micro-bacillus" (p. 35).

Sabouraud discusses at length seborrheic eczema of Unna. He gives Unna credit for having observed the sequelae of the two forms of pityriasis in the scalp but says that he was at fault in ascribing these changes to his morococcus. "The synthesis which he made was in every way remarkable, and the only reproach which one can make is the insufficient description of his microbe and the insufficient differentiation with the other cocci of the skin. It is by reason of the paucity of his bacteriologic methods that so many errors survived" (p. 38). The morococcus, according to Sabouraud, was nothing more than various kinds of staphylococci. "From then on all pustules were declared by him morococcic and little by little the field of seborrheic eczema extended indefinitely." Unna also failed to realize that in pityriasis simplex or steatoides a secondary infection might occur to account for this weeping and crusting. "This superinfection Unna still insisted was seborrheic eczema and he failed to recognize the fact that it was a transitory secondary streptococcic infection" (p. 44). "About the seventeenth year one may see the seborrheic infection of the temples invade the scalp about the borders, beneath the scales of the pityriasis, and one is confronted by a complexus of three infections: the spore of Malassez, the polymorphous coccus and the micro-bacillus. In this way seborrhea of the scalp begins."

In the discussion of the treatment of hypertrichosis it is interesting to note what is said concerning the use of thallium acetate. "The local use of thallium acetate has been much criticized in recent years. It was one of us (Sabouraud, Entretiéns dermatologique à l'École Lailler, 1re série) who suggested it twenty years ago and we have never seen its use followed by accidents. But we must know how and when to use it and also the results one may expect. Never can one expect to obtain more than one-half diminution of the existing hypertrichosis. The disgrace thereby becomes only half as visible, but when it is slight the result is sufficient. A pomade of acetate of thallium should never exceed 2 per cent and never should the patient use more than the size of a small pea in all. It is applied by massage over the region. After the massage the hands are washed with soap. . . . This treatment should be repeated each evening. For three months the results may seem negligible but each month thereafter there is improvement."

In some ninety-two pages the entire subject of alopecia, including pelada and pseudopelada, is discussed. Much of this material is to be found in Sabouraud's book on the alopecias (Pelades et alopécies en aires, Paris, Masson & Cie). As he is the recognized authority on alopecia areata, it is refreshing to read the closing sentence: "All of which proves that there remains much to learn on the subject."

Audry, who has since passed away, discusses the disorders of the sweat glands. Following this is a dissertation by Chatellier on hydrosadenitis, granulosis rubra nasi and anidrose avec hypotrichose et anodontie.

The diseases of the nails are treated at length by Milian. The subject is so well covered and the illustrations are so admirable that no comment is necessary. The chapter should serve for years to come as an authoritative reference on onychia.

Gastinel and Solente give a highly satisfactory presentation of erythema multiforme with magnificent illustrations in color as well as in monochrome. Following this Solente describes érythèmes figurés chroniques. This most difficult group of dermatoses is handled in a masterly way and is accompanied by excellent illustrations and five pages of bibliography.

Dermatitis herpetiformis is well set forth by Tzanck and Cord and is followed by an article on hydroa vacciniforme by Tzanck and Pautrat. This group is ended by Lévy-Solal and Pautrat on herpes gestationis.

A feature of this volume is the work of Pautrier on lichen planus and abnormal lichenification. Those who are familiar with the voluminous contributions made by this author to the subject need not be told that he has completely covered these dermatoses in the 130 pages. There are sixteen plates in color illustrating his original investigations made on lichen planus. Any further comment on the work of this author would be superfluous.

To Margarot falls the responsibility of covering the subject of psoriasis. In the 112 pages allotted to him he gives an excellent account of his ability. The illustrations and the bibliography added to a particularly clear style of exposition make this part of the volume most admirable. The description of psoriasis arthropathique is the most satisfactory that comes to mind. There are three roentgenograms which contribute greatly to the clear understanding of this complicated feature of psoriasis.

Cohen writes an excellent exposition on pityriasis rubra pilaris in a few pages. The two illustrations, one in monochrome and one in color, are strikingly accurate.

Another feature of this volume is the contribution of Civatte on parapsoriasis. The bibliography is scanty but the photographs both clinical and micrographic are numerous and of the highest quality. The exposition, as is to be expected of Civatte, is perfect.

The exfoliating erythrodermas by Nanta and urticaria pigmentation by Gastou are complete in every way.

The most arresting feature in this volume is the closing 141 pages by Henry, professor of parasitology and dermatology of the veterinary school of Alport and Bory of Saint-Louis on comparative dermatology. Their opening statement is as follows: "We define comparative dermatology as the study of animal dermatoses which may have something in common or comparable with human dermatoses, taken as a point of departure or of return." The authors discuss successively the parasitic dermatoses due to insects, Acarus, Demodex, scabies, cutaneous worms, protozoans, Epidermophyton, Trichophyton and all the other diseases common to man and animal. The illustrations and the bibliography are of the highest order. No one should neglect an opportunity to read intensively this section of volume VII.

**Clinics on Secondary Gastro-Intestinal Disorders: Reciprocal Relationships.** By Julius Friedenwald, M.D., Theodore R. Morrison, M.D., Clinical Professor of Gastro-Enterology, University of Maryland School of Medicine, Baltimore, and Samuel Morrison, M.D., Assistant Professor of Gastro-Enterology, University of Maryland School of Medicine, Baltimore. Cloth. Price, $3. Pp. 251. Baltimore: William Wood & Company, 1938.

Any book that bears the name of Julius Friedenwald will be read with interest and respect by his colleagues, who know that he has had an enormous experience and that in spite of his years he remains young in outlook on science and life. This book was written primarily for the medical student and general practitioner, the idea being to put together a few essays on some of the conditions outside the stomach and intestine which commonly produce indigestion. Among these are heart disease, pulmonary tuberculosis, liver and gallbladder disease, focal infection, genito-urinary disease, disease of the female pelvic organs, endocrine dysfunctions, menopausal upsets, syphilis, hematopoietic and dietary deficiency disturbances, nervous disturbances, skin diseases, eye diseases and food allergy.

On looking through the book one finds much that is interesting and much that is sane and helpful. There are good bibliographies at the end of the chapters. Obviously in a short book like this the expert will always see gaps and places in which he thinks he could have written more, chosen the subject matter more wisely or quoted better authorities. The principal criticism that might be made is that in a number of places the information given is not sufficient so that the physician seeking information can gain clearcut impressions of the essential points which will help him in diagnosis or guide him in treatment. For instance, in the section on heart disease there is a good deal about the easily recognized disturbances of digestion which go with decompensated valvular heart disease. Actually, where a physician needs help most is in attempting to recognize the digestive disturbances produced by a narrowing coronary artery some time before the patient drops dead. What is needed is help in differentiating gas in the splenic flexure that is pressing up on the heart from the sensation of gas that is being produced by a failing heart.

On the whole, however, the book is interestingly and well written and contains much information. It should be on the shelf of every man who is trying to fit himself to be a better gastro-enterologist. One of the surest signs of a poor specialist is a tendency to accept everything as grist to his mill and to assume that the symptoms complained of by all patients who come to him are due to disease in his pet organ. Conversely, the surest sign of a good specialist and one who has attained unto wisdom is a readiness to say to many patients "Your symptoms may be in my field, but their source is not. Go you out unto another specialist to whom I shall direct you." This little book is designed to help in the development of wise gastro-enterologists.

**Ulcera gástrica y duodenal: Estudio clínico y radiológico. Especialmente de las alteraciones patológicas de la mucosa gastroduodenal. Tercera edición. Por Jose Mª. Oviedo Bustos, adscripto a la Cátedra de clínica médica. Prólogo del Dr. Mariano R. Castex, miembro de la Academia nacional de medicina.** Cloth. Pp. 674, with 510 illustrations. Buenos Aires: Librería y editorial "El Ateneo," 1938.

This large volume is another one of the valuable contributions to modern medicine which emanate periodically from the Medical Clinic of the National University at Buenos Aires under the leadership of Professor Castex. After certain general considerations, the author discusses the various theories of the cause of duodenal ulcer and its frequency and predisposition, anatomy, physiology and symptomatology. Some 240 pages are devoted to the radiologic study of gastric and duodenal ulcer. The remainder of the book deals briefly with gastroscopy and at some length with complications of gastroduodenal ulcer, its diagnosis, prognosis and treatment, nonsurgical and surgical. Finally consideration is given to the hygiene of the gastrectomized patient and the diagnosis and management of some of the complications. Perusal of the text does not reveal any innovations; there is a complete and satisfactory discussion of standard medical conceptions and practice in the management. Many of the radiologic illustrations are amplified by drawings. All the illustrations are clear. One finds the text ample and reliable. The radiologic symptoms are everywhere correlated with the other symptoms and signs. The work constitutes a real clinical contribution which should redound greatly to the credit of the author and to the eminent Argentine clinic which made this extensive work possible.

**A Text-Book of Pathology. Edited by E. T. Bell, M.D., Professor of Pathology in the University of Minnesota, Minneapolis. Third edition.** Cloth. Price, $9.50. Pp. 894, with 414 illustrations. Philadelphia: Lea & Febiger, 1938.

The new edition of Bell's textbook has been thoroughly revised and 123 pages of new or corrected material, forty-eight illustrations—mostly excellent photomicrographs—and more bibliographic references have been added. As in the 1934 edition, the first part of the text is concerned with general pathology, the rest with the pathology of special organs. The same four collaborators have contributed chapters on special subjects. The Mycoses by J. S. McCartney, M.D., is a good brief discussion of the common fungous diseases, and material on moniliasis has been added. McCartney also contributed the chapter on diseases of the liver and gallbladder, which includes new material on infectious jaundice and von Gierke's disease. The chapter on diseases of the spleen, by C. J. Watson, revised by Bell, gives a useful classification of splenic disorders, prefaced by a discussion of splenic functions and anatomy. The discussion of diseases of the heart by B. J. Clawson has a good summary of our present knowledge of rheumatic heart disease, a subject to which its author has devoted special study. Some readers might object to the grouping of malignant and ulcerative endocarditis with endocarditis lenta in the discussion of subacute bacterial endocarditis. The statement is made that death often occurs in coronary sclerosis without thrombosis, but there is no mention of the mechanism stressed by Leary, rupture of an atheromatous plaque with embolization of multiple branches, which may account for some of these fatalities. Diseases of the Blood is an excellent chapter by an expert hematologist, Hal Downey. The material on the erythrocytes and the anemias has been brought in line with recent work. Nonleukemic disorders with quantitative and qualitative changes in the blood cells are well discussed. The section on the leukemias is simple, brief and helpful. Perhaps the lack of confusing detail is explained by the final section on the origin and relations of the blood cells, with its lucid criticism of rigid hematologic classifications. Bell's own contribution—and the major part of the book—has been carefully revised. Among the many subjects treated with greater detail are constitutional and hereditary factors in disease, calcium and chloride metabolism, the pathology of vascular diseases, endocrine disorders and virus diseases. The general discussion of tumors is good. Much new material has been interpolated in the various chapters and there are at least brief accounts of many of the rarer or recently identified conditions, such as nontropical sprue, regional ileitis, lipoid pneumonia and glomus tumors. Especially valuable, coming from a man who has studied renal pathology so thoroughly, is the chapter on diseases of the urinary system. This is prefixed by an excellent discussion of pathologic physiology. The revised classification and discussion of renal diseases is good from both the morphologic and clinical-pathologic points of view. Probably it will not meet universal approval, and Bell himself may wish to make further revision in the next edition. However, this is a real contribution toward clarifying a very confused subject. Considered as a whole, this improved textbook with its expanded bibliographic material should prove a convenient and remarkably complete brief reference work and will probably find considerable use as a textbook for students. The relatively greater emphasis on systemic pathology and the briefer discussion of general pathology and pathologic principles perhaps will bar widespread employment as a beginner's textbook. This balance however makes it a more useful textbook for the advanced student and the practitioner.

**Action hypoglycémiante de l'insuline chez le chien sous l'influence de la pancréatectomie, de la cholédocotomie suivie de pancréas après ligature des canaux et de jeûne prolongé. Par Raymond Castagnou, docteur en pharmacie.** Paper. Pp. 154, with 36 illustrations. Bordeaux: Imprimerie E. Drouillard, 1938.

Dr. Castagnou's monograph describes a number of excellently planned and executed experiments on the hypoglycemic action of insulin on dogs. The study is in several parts. The first is devoted to the investigation of the characteristics of hypoglycemic curves in the normal dog after intravenous and subcutaneous injection of insulin. In executing these, as well as in the subsequent experiments, the author made use of the method devised by Trinquier and modified by Aubertin. He also describes a new measure for the intensity of the hypoglycemic reaction to injected insulin, which is intended to supplement the index of assimilation of Norgaard and Thaysen. This is the angle formed by lines drawn tangent to the assimilation and restoration curves.

A second series of experiments concern themselves with the variations in the hypoglycemic action of insulin, after partial or total pancreatectomy. The principal result here is the observed regularity of the assimilation curves which follow the operation, in contrast to the frequent oscillation observed in similar curves for the normal dog. The pancreatectomy influences all the measures of the hypoglycemic reaction except the relative percentage of fall from the initial blood sugar content to that of the maximal drop after insulin injection. This percentage of drop in the assimilation curve seems to be constant whatever the initial values, and the author's inference from this is that the hypoglycemic action of insulin is related principally to the time during which the insulin continues to act.

In order to determine whether hypoglycemic reaction of insulin might not be linked with the external pancreatic secretions, several experiments involving ligation and section of the pancreatic ducts were made. Results showed that retention of the external secretions in no way influenced the exogenous action of insulin. The author concludes from this that the increased hypoglycemic action of insulin after removal of the pancreas cannot be ascribed, as others have held, to the suppression of the external secretions of the pancreas. The author is likewise of the opinion that in normal conditions also the external pancreatic secretions do not exercise any considerable influence as a regulatory mechanism of the secretions of the organ.

Animals deprived of their glycogen reserve, as a result of fatty degeneration of the liver or of prolonged inanition, fail to show normal hypoglycemic curves. There is an entire lack

of demarcation between the primary and secondary restoration curves. This is explained as due to the impairment of the mechanism which normally excites islet secretion.

The author offers a number of explanations with regard to the causes of various hypoglycemic reactions following injection of insulin, and a new hypothesis as regards their possible bearing on the diabetic mechanism. As regards the latter, Dr. Castagnou suggests that diabetes does not impair the processes, per se, which mediate hypoglycemia but merely retards, for a considerable time, the rate at which these take place. It is the latter secondary fact which accounts for the prolonged action of insulin in diabetes.

The monograph is documented with 108 references to current literature.

**Glaister's Medical Jurisprudence and Toxicology.** Edited by John Glaister, M.D., D.Sc., Barrister-at-Law, Regius Professor of Forensic Medicine, University of Glasgow. Sixth edition. Cloth. Price, $8. Pp. 747, with 115 illustrations. Baltimore: William Wood & Company, 1938.

Sooner or later every active medical practitioner may be called as a witness to render such service as the law may demand from him. Every medical man, therefore, should know what legal demands may be made on him and the more relevant facts on which he may be called to express opinions. This volume provides a dependable guide. The more noteworthy chapters are those devoted to cases of homicide, causes of insensibility, lunacy, insanity, monoxide poisoning and incest. The section on toxicology is complete. Fundamentally and in principles the entire book is sound in all its comment and instruction. Written by an English author experienced in British procedures and courts, he has devoted much space to the quotation of English laws and procedures. These are of course not applicable in this country. The American physician must therefore go further and supplant American laws for the quoted laws. However, there is so much of value presented clearly and correctly that the book is valuable for physicians in this country. It will also reveal the lag in forensic medicine and the need for prompt reforms in our country.

**Le traitement radiologique de Pactinomycose.** Par Axel Reuander. Communication du Radiumhemmet et de l'Institut roentgen de l'Hôpital Serafimer, Stockholm. Cloth: MM. G. Forssell et E. Berven. Acta radiologica, Supplementum XXXV. Paper. Price, 8 Swedish crowns. Pp. 75. Stockholm: P. A. Norstedt & Söner, 1937.

An excellent historical account of our knowledge of actinomycosis is afforded in this monograph, which deals with the localization of the disease and the various methods of treatment, especially with potassium iodide. Credit is given to Bevan for the first case in which treatment was given with the x-rays. In 1905 Bevan described six cases of actinomycosis treated successfully with the roentgen ray. Since then numerous authors have reported favorably. Fifty-two verified cases of actinomycosis treated by Forssell and his colleagues in Stockholm between 1915 and 1932 form the basis of this work. Forssell's technic is given in detail, both for x-rays and for radium. Radium was never used alone but as an adjunct to roentgen treatment. Cure was obtained in 83 per cent of the cervicofacial lesions and in 38.3 per cent of the abdominal cases. There were no survivals among the genital or thoracic cases. Potassium iodide did not seem important as an additional method of treatment; there was no difference in the rapidity of cure in cases in which potassium iodide was not prescribed.

**Kurs rentgenologii (Dlya vrachey i studentov).** Pod redaktsiey Prof. S. A. Reynberga. [Text Book on Medical Roentgenology for Physicians and Students.] Cloth. Price, 14 rubles. Pp. 784, with 580 illustrations. Moscow & Leningrad: Gosudarstvennoe Izdatelstvo biologicheskoy i meditsinskoy literatury, 1938.

This is a textbook on medical roentgenology written for the general practitioner and the medical student. It contains a discussion of the physics of the roentgen rays, the principles underlying the roentgen technic and roentgenologic investigations. There are chapters on the general and the local roentgenologic diagnosis as related to pathologic anatomy, physiology and clinical knowledge. The text further contains a discussion of the biologic properties of roentgen rays and of the principles of general and local roentgenotherapy. The text does not attempt to be anything more than a guide for the medical student and for the general practitioner and, at best, an introduction to the study of roentgenology for the future specialist in this field. As such it is quite satisfactory and fills a gap in the armamentarium of the Russian physician.

**Die tuberkulöse Lungenblutung: Entstehung, Klinik und Behandlung.** Von Dr. med. Friedrich Hasselbach, Oberarzt. Nr. 67, Tuberkulose-Bibliothek, Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- und Obermedizinalrat, Berlin, und Dr. Karl Diehl, Dirigierender Arzt, Sommerfeld. Paper. Price, 6.60 marks. Pp. 43, with 31 illustrations. Leipzig: Johann Ambrosius Barth, 1938.

Most of the illustrations are made from roentenograms of chests. The author discusses the types of hemorrhage of pulmonary tuberculosis with reference to the source of blood and also presents the pathologic changes and theories concerning hemoptysis. With reference to the time of year, he finds that most hemorrhages occur in December. They are also frequent in April and July. The effects of various substances, such as tuberculin, insulin and vitamin C, are discussed, as well as treatment by artificial pneumothorax, rest, sedatives and other usual methods. He calls attention to the fact that pulmonary hemorrhage may be the first external evidence of tuberculosis in the group he classifies as inflammatory or allergic lesions. This work contains a good bibliography, and all the material is well presented.

**Hernia: Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis, and the Operative and Injection Treatment.** By Leigh F. Watson, M.D., Member of Attending Staff of California Lutheran Hospital and Methodist Hospital of Southern California, Los Angeles. Second edition. Cloth. Price, $7.50. Pp. 501, with 281 illustrations. St. Louis: C. V. Mosby Company, 1938.

This edition fulfils the need for an authoritative work on the new developments in the treatment of hernia. The treatment by injection is covered in detail. No extravagant claims are made for the injection method. The indications outlined as to the applicability of the injection method are conservative and conform with the best opinions on this subject. The technical steps are clearly outlined, particularly in the use of the injection method in inguinal and umbilical hernias. For completeness the author has described the technic of the treatment of femoral and incisional hernias by injection but properly does not encourage its use in these types of hernia. A chapter on trusses, while not as complete as might be expected, covers the essential points of good truss fitting. The description of operative technics is excellent. The more popular procedures in the operative treatment of every type of hernia are carefully and accurately described and illustrated by many fine drawings. The use of local anesthesia is advocated and the steps in the induction of such anesthesia are well outlined. There is an excellent chapter on the medicolegal and industrial aspects of hernia. A complete bibliography at the end of each chapter makes this book particularly attractive for the medical student. Throughout the entire book it is evident that the writer has the point of view of the general practitioner, doing limited surgery on hernia, as well as that of the surgical specialist who desires a complete reference work. This book should be a valuable addition to the library of the medical student, the general practitioner and the surgical specialist.

**Handbook of Practical Bacteriology: A Guide to Bacteriological Laboratory Work.** By T. J. Mackie, M.D., D.P.H., Professor of Bacteriology, University of Edinburgh, Edinburgh, and J. E. McCartney, M.D., D.Sc., Director of Research and Pathological Services, London County Council. Fifth edition. Cloth. Price, 9s. Pp. 536, with illustrations. Baltimore: William Wood & Company, 1938.

This little guidebook to bacteriologic laboratory work is now in the fifth edition since 1925. Many useful technics are described, including the care of animals and the methods of animal inoculation and necropsy. One appendix describes methods of filtration and the other the scheme of colors for identifying sugar mediums.

**Epilepsiya.** Pod redaktsiey Kh. G. Khodosa. [Epilepsy.] Paper. Price, 5 rubles. Pp. 239. Irkutsk: Irkutskoe Oblastnoe Izdatelstvo, 1938.

The material embraces cases of epilepsy treated between 1921 and 1933. The monograph deals with clinical aspects of the disease and offers neither new observations nor new theories.

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Liability of Hospital for Improper Treatment by Layman.**—Hendrickson had a sore on his lower lip, which, according to the reported decision, had been a small superficial cancer that had been cured by treatment at several hospitals. He continued to suffer, however, from the after effect of the radium treatment which he had received. Rigley, a layman, arranged a meeting with Hendrickson and told him he could cure the "crab" on his lip in thirty-one days. He claimed he had brought over from Ireland an old family remedy for the cure of cancer, a salve, and displayed Irish newspaper accounts of cures allegedly accomplished by its use. He displayed also a bottle which he said contained a cancer that had been removed from the face of one Smith, at whose home the meeting was held by Rigley's contrivance, although later the court said that there was no evidence that Smith ever had a cancer.

Hendrickson then consulted a physician, a relative, who advised against any treatment except treatment at a hospital and under a physician's supervision. Rigley, however, caused Hendrickson to be examined by a Dr. Hodkin, who later became one of the defendants. He, according to the published decision of the court, after a superficial examination informed Hendrickson that his case was a serious one and that a cure would cost $10,000, which amount he later reduced to $3,000. Hendrickson was subsequently admitted to the defendant hospital, operated by the Park East Operating Corporation, and there Dr. Hodkin introduced Rigley to the superintendent as "the man who has the cure."

There, in the presence of Dr. Hodkin, Rigley ground up a substance, later shown to be an arsenic compound, and made a paste. Because Dr. Hodkin disagreed with Rigley as to the exact area to which the paste should be applied, he left the room and did not return for two weeks. After Dr. Hodkin's departure, Rigley scratched Hendrickson's chin until blood appeared and then applied the paste and covered it with a bandage. He told a nurse employed by the hospital, to whom he admitted he was not a doctor, that the paste "contained white arsenic and herbs; that it was the most powerful poison in the world, but that his herbs controlled it." Two or three days later Hendrickson's face became swollen and painful. Rigley then "put new skin on the lip where the abrasion was in an effort to stop the flow of saliva." On Rigley's instructions, the nurse administered aspirin and whisky to relieve the pain. On one occasion a hemorrhage had to be stopped by a house physician. The paste, which medical witnesses believed should not have been allowed to remain on longer than eighteen hours, was kept on for twenty-one days. When Hendrickson left the defendant hospital, at the superintendent's request, because his hospital bill was not paid up to date, "the flesh had been eaten away from the lip and chin," "there was no lip or chin left, and his teeth fell out."

Hendrickson brought suit and obtained a judgment for $40,000 against the defendants, Rigley, Dr. Hodkin and the hospital. On appeal by the defendant hospital, the supreme court of New York, appellate division, second department (250 App. Div. 619, 294 N. Y. S. 982, abstracted, THE JOURNAL, Jan. 1, 1938, p. 74), reversed the judgment against the hospital. Hendrickson thereupon appealed to the Court of Appeals of New York.

The medical testimony, said the Court of Appeals, showed that the treatment administered by Rigley was a competent producing cause of the appellant's condition. Furthermore, the evidence presented by Hendrickson, the appellant, justified the jury in finding that the hospital admitted the appellant "knowing that the purpose of his being there was for an improper treatment by a layman, 'the man who has the cure';" that the hospital records showed that Rigley personally treated the appellant; that nurses, hospital physicians and the superintendent of the hospital knew that the appellant was being treated by Rigley without the supervision of a physician; that the superintendent knew that the paste used in the treatment was a preparation whose composition was known only to Rigley; and that the superintendent, knowing what was going on, stated: "We will have to play along with him [Rigley]. If everything comes out all right, we will be all taken care of." The superintendent knew or should have known that Rigley was engaged in the commission of a crime by unlawfully practicing medicine, a crime of which he was later convicted, and that the hospital, in affording its facilities for pay, was aiding and abetting him in the performance of a criminal act. The basis of the liability was not the negligence of the doctor or nurse in charge but the wrongful conduct of its superintendent, acting within the scope of his authority, in permitting the facilities of the hospital to be used for the commission of criminal acts in violation of a duty owed to the patient.

In the judgment of the Court of Appeals, the supreme court, appellate division, erred when it held the hospital not liable on the theory that the only fault was that of the doctor and nurse. Accordingly, the Court of Appeals reversed the judgment of both lower courts and granted a new trial.—*Hendrickson v. Hodkin et al. (N. Y.), 11 N. E. (2d) 899.*

**Workmen's Compensation Acts: Compensability of Cerebral Hemorrhage Following Exertion.**—Neas, suffering from high blood pressure, in the course of his employment as a lineman for a power company climbed and descended two poles in rapid succession. After descending the second pole he staggered toward his truck and slumped down in the seat. He was immediately taken to a hospital, where he died within a few hours of a cerebral hemorrhage. The claimants, his wife and children, denied compensation under the workmen's compensation act by the industrial accident board of Texas, filed suit in a state court to set aside the board's award and to recover compensation, but the suit was removed to the federal district court. All the medical witnesses agreed that the cause of death was a hemorrhage due to a rupture of weakened arterial walls in the brain. They agreed that physical exertion would cause an increase of blood pressure and could precipitate such a hemorrhage but that such a hemorrhage could occur without previous violent exertion. In answer to hypothetical questions some physicians expressed the opinion that the climbing and descending of two poles in succession could and did cause the hemorrhage to begin immediately, while others thought that because such exertion was habitual to the workman in this case it did not cause the hemorrhage. From a verdict by the jury in favor of the claimants and from the resulting judgment, the insurer appealed to the circuit court of appeals, fifth district.

The main question was whether the evidence authorized submission of the claim to the jury. The jury, said the circuit court of appeals, could find from the evidence that the workman climbed the two poles in immediate succession and that his hemorrhage was precipitated by that exertion. The hemorrhage, though not outwardly visible, was a "damage or harm to the physical structure of the body" within the meaning of the term "injury" as defined in the Texas workmen's compensation act. The act requires that the injury shall have originated in the work of the employer while the employee was engaged in it, but the jury could reasonably find that the climbing of the two poles was the direct and immediate cause of the arterial rupture and that that rupture would not have occurred but for such exertion.

The insurer argued, however, that in order to recover under the Texas workmen's compensation act there must be an accident in the course of work, something that unexpectedly causes unusual exertion and overstrain, and that there was nothing to show that anything of the sort occurred. But, said the circuit court of appeals, the Texas workmen's compensation act does not expressly require that an accident shall have happened. This very court, in *Salinas* v. *New Amsterdam Casualty Co.*, 67 F. (2d) 829, used the expression "accidental injury," describing such an injury as one occurring unexpectedly and not in the natural course of events and susceptible of being traced to a definite time, place and cause. The arterial injury which happened to Neas was not a wilful injury, was unexpected and not in the usual course of events and was traced to a definite time, place and cause. The test is not whether the exertion or strain which immediately caused the injury was unusual in the course of the work in which the injured employee was engaged

but whether such exertion was beyond that which members of the public not so employed ordinarily would incur. If exertion was not unusual in the latter sense, the employer is not to be charged with the injury even though it happened while the employee was at work. If, however, the employee as a member of the public would ordinarily not incur such a strain as that which injured him, the injury is to be attributed to his employment even though a disease condition may have made him more vulnerable. In this case Neas was required by his employment to climb poles, involving an exertion far greater than members of the public would ordinarily undergo. If that exertion then and there caused a brain hemorrhage which would not have otherwise happened, there was an injury originating in the work for which the statute requires industry to make compensation.

The judgment in favor of the claimants was accordingly affirmed.—*Fidelity & Casualty Co. of New York v. Neas, 93 F. (2d) 137.*

**Adjudication of Insanity: Right to Trial by Jury.**—The appellant was adjudged insane by the commissioners of insanity of Monroe County, Iowa, and ordered committed to a state hospital. She appealed to the district court of that county and from an order of the district court denying her a trial by jury she appealed to the Supreme Court of Iowa, contending that that denial invaded her right of trial by jury guaranteed by the constitution of Iowa.

The purpose of an inquisition of insanity, said the Supreme Court, is to aid and assist the individual, to provide means whereby the state may protect its unfortunate citizens and to furnish hospitalization and treatment in order that the insane may have an opportunity to rehabilitate and readjust themselves as useful and happy citizens. Such an inquisition is not a criminal proceeding in any way. Confinement of persons who are mentally sick is not intended as punishment but only to provide them with an environment that may possibly cure their disease and return them to society. Accordingly, the Supreme Court, two justices dissenting, affirmed the judgment of the lower court, denying the appellant the right to a trial by jury. —*In re Brewer (Iowa), 276 N. W. 766.*

**Workmen's Compensation Acts: Liability for Expense of Exploratory Operation.**—On January 7 Bochat, while shoveling snow from the roof of a shed in the course of his employment by the defendant, slipped and fell. He sustained "a back sprain," which healed by February 20. From ten to thirty days after his fall he noticed pain and swelling on the right side of his abdomen. His condition became progressively worse and an immediate operation was recommended. His attending physicians were of the opinion that the operation would prove or disprove their belief that his condition was not due to the accident. Bochat was informed that the industrial commission would assume all costs "if it appeared, after the operation, that his condition was caused, or aggravated, by the accident," but that if it appeared that his condition was not attributable to the accident he would have to bear the costs. The operation was performed and a hydronephrosis of one kidney was found. This, the operating physicians concluded, had been present long before the accident and had not been aggravated by it. The claimant brought proceedings before the industrial commission under the workmen's compensation act of Arizona. From an award of the commission granting compensation for temporary disability from January 9 to February 20, the period during which he suffered from a strain of his back, but denying compensation for any time thereafter, he appealed to the Supreme Court of Arizona.

If it appeared from the record, said the Supreme Court, that the operation had been performed at the request of the commission to satisfy it as to the cause of the claimant's condition, the court would be inclined to hold that the commission was liable for the expenses caused by its request. The evidence did not show, however, that the operation had been performed at the commission's request. The situation prior to the operation was that on the information then available to it the commission would have had to deny any request for compensation further than that which it had awarded. An operation was necessary to save the claimant's life regardless of the cause of his condition. On this state of the affairs the commission went as far as it had any right to go when it informed the claimant that it would pay the expenses of the operation *if it revealed that the accident had caused or aggravated his condition.* Since the testimony of the operating physicians showed that the accident had not caused or aggravated the claimant's condition, the court concluded that the commission had properly refused to award additional compensation. Accordingly, the award of the industrial commission was affirmed.—*Bochat v. Prescott Lumber Co. (Ariz.), 74 P. (2d) 575.*

**Workmen's Compensation Acts: Death Caused by Exertion and Myocardial Disease Compensable.**—The deceased, a carpenter, in the course of his employment assisted his fellow workmen in lifting and carrying window sashes and lumber, the individual pieces ranging in weight from 75 to 100 pounds. The thermometer stood at 90 F. in the shade, and the men worked in the sun's rays and under pressure. The deceased seemed to be exhausted. He perspired very freely and a fellow workman had "to keep pushing him along." He went into the cellar to get a drink of water. Five minutes later he was found unconscious and shortly thereafter he died. His widow sought compensation under the workmen's compensation act of New Jersey.

A physician testifying on behalf of the widow said that the death, caused by "syncope due to myocardial heart disease," was the result of the exertion incident to employment. A physician testifying on behalf of the employer stated, however, that while he believed that death was due to heart disease he could find no evidence of any accident and that the exertion of employment had no relation to the death. On cross examination he admitted that the exertion "may have been more liable to have something to do with it" and that exertion will aggravate a myocardial condition. Another physician called by the employer admitted that, when heart disease exists, such exertion as that of the deceased, coupled with the extreme heat of the day, could cause death. The workmen's compensation bureau nevertheless denied compensation, holding that the claimant had failed to prove that her husband died as the result of an accident arising out of and in the course of his employment. She appealed to the court of common pleas, which reversed the decision of the workmen's compensation bureau and awarded her compensation. The employer thereupon brought certiorari to the supreme court of New Jersey.

Unquestionably, said the supreme court, the deceased workman had a preexisting heart disease. While the testimony indicated that he might have died at any time, there was also testimony supporting the conclusion that there was a causal relation between the death and the heavy work in which the deceased was engaged, the extreme heat of the day and more or less continuous exertion. The employer stressed the fact that the work done by the workman was the same work as was done by others and therefore was not unusual. This argument, said the court, is without merit, since the proofs support the conclusion that the workman showed symptoms of having been subjected to unusual exertion. The supreme court accordingly affirmed the award in favor of the widow.—*Schneider v. F. & C. Haerter (N. J.), 197 A. 281.*

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## Society Proceedings

### COMING MEETINGS

American Society of Tropical Medicine, Oklahoma City, Nov. 15-18. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.

American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.

Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Society of American Bacteriologists, New Haven, Conn., Dec. 28-30. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.

Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.

Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American Journal of Cancer, New York

34: 1-168 (Sept.) 1938

Observations on Chorionepithelioma Testis: Record of Case. S. McDonald Jr., Birmingham, England.—p. 1.
Carcinoma of Kidney in Leopard Frog: Occurrence and Significance of Metastasis. B. Luché, Philadelphia.—p. 15.
Leiomyoma of Oral Cavity. A. P. Stout, New York.—p. 31.
Carcinogenic Activity, Structure and Chemical Reactivity of Polynuclear Aromatic Hydrocarbons. L. F. Fieser, Cambridge, Mass.—p. 37.

### American Journal of Clinical Pathology, Baltimore

8: 471-596 (Sept.) 1938

*Early Diagnosis of Acute and Latent Plumbism. F. L. Smith 2d, T. K. Rathmell and G. E. Marcil, Philadelphia.—p. 471.
Monocytic Leukemia, with Analysis of Cell Characteristics by Supravital and Fixed Staining Technics. Regena Cook Beck, Richmond, Va.—p. 509.
Lyophile Complement in the Kolmer Complement Fixation Test for Syphilis. J. A. Kolmer, Carola E. Richter and Elsa R. Lynch, Philadelphia.—p. 522.
Flocculate Induced Antibodies and Syphilis Immunity in Rabbits. F. Rytz, Minneapolis.—p. 529.
*Serum Cholesterol Fluctuations During the Menstrual Cycle. F. M. Offenkrantz, with cooperation of Anne M. Staniel, Newark, N. J.—p. 536.
Histologic Study of Endometrium During Pregnancy. A. C. Broders and J. R. McDonald, Rochester, Minn.—p. 547.
Primary Carcinoma of Hepatic Ducts: Case Report. L. H. Snyder, Washington, D. C.—p. 563.
Leukemia in the Newborn, with Death at Birth from Traumatic Rupture of Spleen. B. W. Rhamy, Fort Wayne, Ind.—p. 567.
Pulmonary Sclerosis. R. J. Jermstad, Washington, D. C.—p. 573.

**Early Diagnosis of Plumbism.**—According to Smith and his associates, a differential diagnosis of lead poisoning can be accomplished by an accurate determination of lead in the serum, cells and fibrin fraction of the blood when taken into consideration with the total amount of lead in the whole blood. It is possible by this procedure to make a differentiation between acute, chronic and mild lead poisoning as well as to differentiate between mild lead toxemia and such pathologic conditions as gastro-enteritis, hypercalcemia, food poisoning, sun and x-ray burns or colics from other causes. The therapeutic use of lead can be controlled by this procedure, since deleading treatment may be instigated before an acute lead crisis develops. Results of 0.001 mg. of lead or less in 10 Gm. of serum, cells and fibrin or whole blood may be in error and should be considered qualitatively rather than quantitatively. Such a consideration does not change the interpretations, as the important factor is the appearance and disappearance of pathologic lead in the serum fraction of the blood. The essential difference in the manner in which the analysis of the blood of healthy persons differs from definite clinical cases of acute lead poisoning and periods of exacerbation in chronic lead poisoning lies in the appearance of lead in the serum fraction of the blood, since approximately 34 per cent of these cases show a whole blood content of less than 0.01 mg. of lead in 10 Gm. of blood and 18 per cent have a whole blood content bordering on the normal range of healthy persons. In thirty-four cases of latent and early acute phases of chronic plumbism there was a definite appearance of lead in the serum fraction of the blood in all the cases although the lead content of the whole blood in 68 per cent was less than 0.01 mg. in 10 Gm. and 44 per cent fell within the limits of the range established by healthy normal persons and patients with disorders other than plumbism. In inactive chronic plumbism the serum is normal but there is usually a definite increase in the lead content of the whole blood over that of the control group. However, a definite diagnosis may be established in borderline cases by placing the patient on acid therapy as practiced in deleading, when an increase in the serum fraction and generally in the whole blood will occur. The clinical and physiologic course of lead intoxication through its quiescent periods as well as those of acute and subacute exacerbation may be followed by means of the analysis of the serum fraction and the whole blood for lead, and a prognosis established. Since it requires 10 Gm. of blood to make a determination for lead by the diphenylthiocarbazone method, the clinical procedure followed in cases complicated by the presence of malignant growths or blood dyscrasia is first to make an analysis of the lead content of the serum, cells and fibrin fraction and whole blood, then follow the trend of the intoxication by means of daily shiftograms and hemograms, and make additional blood analyses when they are hemographically or clinically indicated. However, in uncomplicated cases an analysis is made every second or third day. By such a procedure it is found possible to differentiate between symptoms caused by mild lead poisoning and those which result from pathologic conditions. A range of lead values for the healthy normal person is found to be nil in 10 Gm. of blood serum, from 0.002 to 0.011 mg. in 10 Gm. of cells and fibrin fraction and from 0.001 to 0.005 mg. in 10 Gm. of whole blood. This range was independent of sex, age, climatic changes, daily fatigue, violent exercise, meals, menstruation and ovulation.

**Serum Cholesterol During Menstrual Cycle.**—Offenkrantz presents data for each of a total of sixteen monthly cycles in sixteen young, healthy and regularly menstruating women. About eight determinations in a cycle were performed. The following facts were observed: 1. There is a sharp elevation of the total serum cholesterol at the end of the bleeding phase, associated with a slightly lowered percentage of free cholesterol. 2. There is a lowered total serum cholesterol at the onset of the menses. The percentage of free cholesterol is higher at this time than at its termination. 3. The intermediary cholesterol levels show a tendency to rise to the middle of the cycle and then fall off toward the new cycle. 4. Although there were wide fluctuations for each subject, no determination was outside the values previously found in other series on normal subjects. 5. There appear to be definite planes (i. e. higher, lower or intermediate levels) along which all the total cholesterol values for any subject will vary. These planes are held to be determined, in part, by the constitutional reaction type of the subject. 6. The narrow limits of fluctuation of the percentage of free cholesterol indicate the importance and stability of this factor. This variation is from 22.09 to 32.9 per cent of the total cholesterol. The meaning of this variation of cholesterol values with regard to the menstrual cycle is discussed.

### American Journal of Diseases of Children, Chicago

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*Intravenous Injection of Hypotonic Salt Solution Containing Sulfanilamide for Streptococcic Meningitis. G. M. Retan, Syracuse, N. Y.—p. 483.
Effect of Milk Supplement on Physical Status of Institutional Children: II. Ossification of Bones of the Wrist. Vera MacNair, Rock Hill, S. C., and Lydia J. Roberts, Chicago.—p. 494.
Sedimentation Rate in Nutritional Anemia of Infants and Children: Its Response to Treatment with Iron (Ferrous Sulfate). C. H. Smith, New York.—p. 510.
Erythrocytes and Hemoglobin of Blood in Infancy and in Childhood: II. Variability in Number, Size and Hemoglobin Content of Erythrocytes During the First Five Years of Life. G. M. Guest, Estelle W. Brown and Mary Wing, Cincinnati.—p. 529.
Human Passive Transfer Antibody: III. Serial Titrations on Treated and Untreated Patients with Hay Fever. W. M. Schmidt and V. W. Lippard, New York.—p. 550.
*Minimal Vitamin C Requirements of Artificially Fed Infants: Study of 427 Children Under Controlled Dietary Regimen. B. M. Hamill, L. Reynolds, M. W. Pooks and Icie G. Macy, Detroit.—p. 561.
*Comparative Study of Tuberculin Patch Test and Mantoux Intracutaneous Test. H. Vollmer, New York, and Esther W. Goldberger, Staten Island, N. Y.—p. 584.
Talmudic Contribution to the History of Diphtheria. A. Bernstein, San Francisco.—p. 612.
Carcinoma of Thyroid Gland in Children: Report of Case Associated with Multiple Anomalies of Development, with Studies of Basal Metabolism, Serum Cholesterol and Creatine Excretion After Thyroidectomy. A. G. Langmann and Hilde Bruch, New York.—p. 616.

**Saline Solution and Sulfanilamide in Meningitis.**—In experiments on monkeys, planned to determine whether giving sulfanilamide intravenously has the advantage of increasing the concentration of the drug in the cerebrospinal fluid, Retan observed that when physiologic solution of sodium chloride

containing sulfanilamide is given to monkeys intravenously the concentrations of sulfanilamide are greater in the blood than in the cerebrospinal fluid. When a hypotonic solution of sodium chloride containing sulfanilamide is injected intravenously, the concentrations during the first injection are the same as with the physiologic solution. However, if the injection of a hypotonic solution is repeated on the second day there occurs a shift to a higher percentage of sulfanilamide in the cerebrospinal fluid than is contained in the blood. A similar shift to higher concentrations in the cerebrospinal fluid than in the blood can be produced by giving the drug by mouth in solution or in capsules prior to the intravenous injection of a hypotonic solution of sodium chloride. The shift depends on the presence of sulfanilamide in the tissues of the body and the intravenous introduction of a hypotonic solution of sodium chloride containing sulfanilamide. The author is not in a position to know what result he should have obtained in his case of hemolytic streptococcus meningitis had he given sulfanilamide by mouth and by subcutaneous injection without using injections of hypotonic solution of sodium chloride containing sulfanilamide. However, every one who saw the patient was impressed by the prompt subjective and objective improvement shown within an hour of the beginning of each intravenous injection. He believes that this method of treatment is based on sound theoretical grounds. It would seem that the doses of sulfanilamide used in the intravenous solution (from 6 to 10 Gm. in twenty-four hours) were unnecessarily large. In his next case he plans to give about half as much sulfanilamide in the hypotonic solution. However, there were no harmful results. An alkaline powder of calcium carbonate and sodium bicarbonate was given at intervals of four hours. The rate of injection most successfully used is 10 cc. of solution each hour per pound of body weight. A 0.375 per cent solution has been found to be most effective. Treatment for five hours with rest intervals of several hours between treatments is advised. Cerebrospinal fluid is released from the lumbar puncture needle during the intravenous injection for the purpose of relieving increased intracranial pressure. If the fluid is under considerable pressure and is spurting from the needle, it is wise to drain from 5 to 10 cc. during half an hour. If the fluid is dripping rapidly, less than this amount should be drained. If the fluid emerges from the needle by a slow drop, the stylet should be replaced at once without draining any fluid. The drainage of too great an amount of cerebrospinal fluid during the intravenous injection of a hypotonic solution of sodium chloride can result in cerebellar herniation.

**Minimal Vitamin C Requirements.**—Hamil and his co-workers studied 427 infants, comprising a cross section of the indigent and near indigent class of Detroit, during their first year of life. Of these 80 per cent were under observation for nine months or longer. The children were in their home environment, and the investigation was closely controlled. Almost 10 mg. of vitamin C was made available to each infant daily by the addition of powdered lemon juice to their formulas. It appeared that the minimal protective dose of vitamin C for the average healthy infant is about 10 mg. daily. Comprehensive examinations of each infant were made monthly or more often. From the data on the 427 infants observed it appears that the condition which has usually been considered latent scurvy is actually definite mild scurvy. It seems that scurvy is a definite pathologic entity but does not become evident or retard development until the absence of the specific physiologic functions of the vitamin is manifest. During the course of the study twenty-one infants had mild scurvy. During the time mild scurvy was present the rates of gain in weight and height were retarded but development in sitting, standing, creeping, walking and talking was not. From the results it appears that an infection predisposes to mild scurvy but is not a concomitant symptom of the condition. Lowering of the hemoglobin level does not appear to be a symptom of mild scurvy nor does it predispose to the development of this disease.

**Tuberculin Patch and Mantoux Tests.**—Of 169 children with active tuberculosis whom Vollmer and Goldberger tested only one of those who reacted positively to the Mantoux test with the stronger solution of purified protein derivative failed to react positively to the tuberculin patch test. Among 118 children admitted in a routine manner to the pediatric service of the Mount Sinai Hospital with various diseases the Mantoux test, even with 1 mg. of old tuberculin, did not reveal a single case of tuberculous infection which was not already discovered by the tuberculin patch test.

## Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

40: 325-484 (Sept.) 1938. Partial Index

Practical Importance of Mechanics in Digestion. A. E. Barclay, Oxford, England.—p. 325.
Experimental Studies on Gastric Physiology in Man: IV. Influence of Osmotic Pressure Changes of Salt and Sugar Solutions on Pyloric Action and Gastric Emptying in Normal and Operated Stomach. J. Gershon-Cohen, H. Shay and S. S. Fels, Philadelphia.—p. 335.
Ventriculographic Localization of Intracranial Tumors: II. Tumors of Aqueduct, Pons and Cerebellopontile Angle. V. C. Johnson, C. F. List, Ann Arbor, Mich.—p. 348.
Enlarged Glomus Defect Contralateral to the Side of Ventricular Puncture: Its Occurrence Due to Cysts of Glomus. M. H. Poppel, New York.—p. 357.
*Shape of the Female Pelvis and Its Clinical Significance: Further Roentgen Studies. L. H. Garland, San Francisco.—p. 359.
Roentgenologic Diagnosis of Perinephric Abscess and Perinephritis. A. E. Goldstein and M. Ostro, Baltimore.—p. 371.
Roentgen Diagnosis of Reducible Hernia. Carye-Belle Henle, Newark, N. J.—p. 392.
Visualization of the Aorta by the Method of Roentgenographic Overpenetration. B. S. Epstein, Brooklyn.—p. 396.
End Results of Irradiation of Thymus Gland in Twenty-Seven Normal Infants and Children. C. G. Kerley, New York.—p. 416.
Some Effects of Radiation on Oil. W. Stenstrom and I. Vigness, Minneapolis.—p. 427.

**Shape of the Female Pelvis and Its Clinical Significance.**—On a morphologic or architectural basis Garland classifies female pelves into four main types: gynecoid, android, anthropoid and platypelloid. In a group of 150 unselected primiparas the incidence of these types was found to be gynecoid 51, android 21, anthropoid 18 and platypelloid 10 per cent. Approximately 79 per cent were pure types and 21 per cent mixed types. The size of the pelvic inlet, the width of the subpubic angle and the shape of certain other anatomic features were carefully measured. These data are of value in arriving at the correct x-ray interpretation but are independently variable within wide limits. The inclination of the pelvic inlet relative to the horizontal, with the patient recumbent, was studied and it was found that in the average case it is approximately 20 degrees (not 42 degrees as reported in the literature). The clinical significance of this observation in connection with certain classic obstetric maneuvers is obvious. With reasonable care the shape of the female pelvis can be readily diagnosed by a set of three roentgenograms, and, especially in the android type, a potentially difficult labor can be forecast in patients whose obstetric measurements by ordinary clinical methods appear normal.

## Annals of Internal Medicine, Lancaster, Pa.

12: 285-428 (Sept.) 1938

The Heart in Pulmonary Tuberculosis: Electrocardiographic Consideration. W. R. Leverton, San Fernando, Calif.—p. 285.
Common Gastrointestinal Emergencies and Their Medical Aspects. G. B. Eusterman, Rochester, Minn.—p. 306.
*Clinical Observations, Complications and Treatment of Acute Upper Respiratory Tract Infections. A. V. Bock, Cambridge, Mass.—p. 317.
Constitutional Factors in Arthritis, with Special Reference to Incidence and Role of Allergic Diseases. R. T. Pottenger, Pasadena, Calif.—p. 323.
Affective Disorders in Medical Practice. T. P. Sprunt, Baltimore.—p. 334.
*Studies on Life Histories of Patients with Chronic Ulcerative Colitis (Thrombo-Ulcerative Colitis), with Some Suggestions for Treatment. J. A. Bargen, R. J. Jackman and J. G. Kerr, Rochester, Minn.—p. 339.
Quinine and Atabrine: A Comparison. O. T. Brosius, Santa Marta, Columbia.—p. 353.
Coronary Artery Disease and Angina Pectoris: Present Status with Review of Some of the Recent Literature. I. C. Brill, Portland, Ore.—p. 365.
The Mechanism of Heat Loss and Temperature Regulation. E. F. Du Bois, New York.—p. 388.

**Infections of Respiratory Tract.**—Bock discusses the care of 1,667 cases of acute infection of the respiratory tract treated by himself and his associates from September 1935 to March 1938. The subjects were undergraduate and graduate students at Harvard, the principal age range being from 17 to 25 years. The main purpose of his discussion is to make a plea for simple treatment, the fruits of which are perhaps best indicated by the relatively small list of complications (twenty-nine cases of otitis media, one of mastoiditis, two surgically drained antrums, one peritonsillar abscess and fifty-two of pneumonia) of all sorts

occurring in this series. Common sense treatment of acute infections of the upper part of the respiratory tract, including the common cold, with or without fever, requires bed care. Whatever the specific etiologic factors may be, it is clear to the author that fatigue of body and mind in adult patients is a factor in the precipitation of these infections not generally recognized. The main principle of treatment should be rest. Energetic local treatment produces irritation of the nasopharyngeal membranes, often prolonging the course. Salicylates and codeine are used for comfort. Laxatives are not usually prescribed. Control of temperature, humidity and dust would add greatly to the effectiveness of treatment. Prevention of infections of the upper part of the respiratory tract by vaccines has little to support it. Lacking specific means of therapy, the greatest advance on the problem at the moment would be made if the physician taught himself and his patients how to live within his and their physical resources, and especially within those of one's central nervous system. Such influences as chilling of the body, weather changes, irritative substances in the atmosphere and contagion must be taken into account; but granting these, under ordinary circumstances, the part played by the tension of living must be recognized more generally in solving the problem.

**Chronic Ulcerative Colitis.**—During the years 1925 to 1931 inclusive Bargen and his colleagues observed seventy-three patients who had tuberculous ileocolitis at the Mayo Clinic, approximately 500 who had amebic colitis, 129 who had ulcerative colitis of undetermined etiology and 871 who had thrombo-ulcerative colitis (of bacterial origin). A statistical study of the records of the 871 patients who had thrombo-ulcerative colitis, followed from seven to fourteen years after the first observation, shows that the predisposing factors and those affecting relapses of the disease are: infections of the upper part of the respiratory tract, disease of childhood, dietary indiscretion, physical and mental fatigue, rectal or abdominal surgery, trauma, drastic catharsis, foci of infection with sepsis, exposure, dysentery epidemics and pregnancy. This disease may begin in an insidious manner. Again it may come on suddenly as a violent diarrhea without toxic symptoms or it may start in a fulminating fashion associated with marked toxemia, fever and all the concomitants of a severe septic process. The major complications and sequelae of thrombo-ulcerative colitis include polyposis, stricture, perianal abscess-fistula, arthritis, erythema nodosum, pyoderma gangrenosa, perforation, hepatic abscess, carcinoma, phlebitis, iritis, deafness, splenomegaly, nephritis, psychosis, massive hemorrhage, endocarditis and renal stones. There is no special time of year in which the disease begins, but more of the cases had their onset in January, February or July than in the other months of the year. The progress of the invasion from the rectum toward the cecum is indicative of its destructive nature. The mortality (at the time of inquiry 19.3 and 12.9 per cent, male and female, respectively) associated with this destructive infection emphasizes its serious nature. Surgical intervention in this disease should be limited to complications and sequelae. Some of these demand wisely chosen surgical measures, both from the standpoint of the time of their application and from that of the lesion present. A person with thrombo-ulcerative colitis presents a poor surgical risk if a surgical attempt must be made to relieve another intercurrent abdominal pathologic condition. Complete relief of all symptoms and signs of intestinal pathologic change occur frequently enough to make it urgent that a well ordered regimen be followed without deviation by these patients for months and years.

## Annals of Medical History, New York

10: 369-462 (Sept.) 1938

Santorio Santorio. R. H. Major, Kansas City, Kan.—p. 369.
Captured Medical Men and Army Hospitals of the American Revolution. J. E. Gibson, Philadelphia.—p. 382.
Sketches of the Life and Interests of Sir Hans Sloane: Naturalist, Physician, Collector and Benefactor. B. Chance, Philadelphia.—p. 390.
L'Hôpital Saint-Louis: Brief Biographic Sketch of Its Early Teachers and Their Influence on American Dermatology. P. E. Bechet, New York.—p. 405.
Eighteenth Century Obstetrics and Obstetricians in the United States. E. M. Jameson, Saranac Lake, N. Y.—p. 413.
Maimonides' Prayer. S. R. Kagan, Roxbury, Mass.—p. 429.
Some Remarks on Keats and His Friends. R. Armstrong-Jones, London, England.—p. 433.
Alexander Porfirivich Borodin: Physician, Chemist and Composer. F. W. Sunderman, Philadelphia.—p. 445.

## Archives of Internal Medicine, Chicago

62: 547-722 (Oct.) 1938

*Action of Digitalis in Compensated Heart Disease. H. J. Stewart, H. F. Crane, J. E. Deitrick and W. P. Thompson, New York.—p. 547.
Action of Digitalis in Uncompensated Heart Disease. H. J. Stewart, J. E. Deitrick, N. F. Crane and C. H. Wheeler, New York.—p. 569.
Clinical Studies of Respiration: VII. Additional Observations Concerning Validity of Results Obtained with Body Plethysmograph. J. A. Greene, L. W. Swanson and R. H. Heeren, Iowa City.—p. 593.
Pneumonia Complicated by Acute Pneumococcic Hemorrhagic Ulcerative Gastro-Enteritis (Dieulafoy's Erosion): Report of Two Cases. C. H. Sanford, J. D. Hughes and J. Weems, Memphis, Tenn.—p. 597.
Diabetes Insipidus as Sign of Metastatic Involvement of Supra-Opticohypophysial System. M. Bernstein, M. T. Moore and D. B. Fishbach, Philadelphia.—p. 604.
*Chemical Factors Concerned in Formation of Gallstones. R. E. Dolkart, K. K. Jones and C. F. G. Brown, Chicago.—p. 618.
Primary Carcinoma of Lung: Clinical and Pathologic Study of 100 Cases. S. Koletsky, Cleveland.—p. 636.
Gastro-Enterology: Review of the Literature from January 1937 to June 1938. C. M. Jones, T. V. Urmy, E. B. Benedict, M. H. Clifford and B. V. White, Boston.—p. 652.

**Digitalis in Compensated Cardiac Disease.**—Stewart and his co-workers gave from 1.6 to 1.8 Gm. of digitalis within twenty-four hours to thirteen patients suffering from rheumatic cardiac disease and to four others with arteriosclerotic, hypertensive or syphilitic cardiac disease. There was compensation, and a normal sinus mechanism was exhibited. In all cases the T wave and the RT segment of the electrocardiogram showed the changes characteristic of a digitalis effect. Seven patients showed a decrease in cardiac output and a decrease in cardiac size, four patients showed an increase in cardiac output and a decrease in cardiac size, and six patients showed no change in cardiac output and in cardiac size. In short, in some instances when the heart was made smaller the cardiac output increased, and in others it decreased. In the former cases the heart behaved like a failing heart and in the latter cases like a normal one. The results in five patients exhibiting auricular fibrillation were not different from those encountered in those with normal sinus rhythm—a decrease in cardiac size was associated with a decrease in cardiac output, and an unchanged cardiac size was associated with an unchanged cardiac output. A few observations on patients with cardiac disease due to other etiologic factors showed that the phenomena of digitalis are not confined to those with rheumatic involvement. There is one phenomenon which is common to all groups: the giving of digitalis increases the work accomplished by the heart per beat, whether its action is to increase or to decrease the output or to leave it unaltered and whether the rhythm is regular or that of auricular fibrillation. As a consequence, work becomes more nearly appropriate for the size of the organ. Some basis is afforded Christian's suggestion of giving digitalis to the patient suffering from organic cardiac disease even though he shows no significant failure. A decrease in cardiac output which follows the giving of digitalis to human beings (normal and those having organic cardiac disease without congestive cardiac failure) is not a consequence of diminished venous return but a consequence of a decrease in the size of the heart due to the action of digitalis.

**Chemical Factors in the Formation of Gallstones.**—According to Dolkart and his associates, in all the various bile salt preparations used in the experiments the sodium salt of pure cholic acid proved to have the greatest cholesterol-solvent capacity, with sodium taurocholate, sodium desoxycholate and sodium glycocholate, in the order named, next in activity. There appears to be an optimal concentration for some of the preparations used. Changes in the structure of the bile acid molecule have a marked effect on the ability of the particular acid to hold cholesterol in solution. Conjugation with aminoacetic acid or taurine somewhat decreases this ability. The oxidation of desoxycholic acid to the keto form resulted in a marked loss of solvent capacity. Mixed ketocholanic acid showed moderate ability to hold cholesterol in solution, and it appears that some additional substance—possibly chenodesoxycholic or lithocholic acid—is present. The authors' results demonstrate that bile salts are not the most essential substances for maintaining cholesterol in solution in the bile. In equivalent concentrations the fatty acids were far more active as cholesterol solvents than were the bile acids. The studies of the cholesterol-solvent capacity of fractions of bile showed that whether or not the animal belonged to a species which forms gallstones, if the bile

was solvent for cholesterol, the solvent capacity could be isolated in the saponifiable or fatty acid fraction. There was a considerable decrease in the amount of this saponifiable fraction in relation to the cholesterol content of the bile in those animals which form gallstones, as compared with the amount in those which never form gallstones. Whether the fatty acids as they occur in the bile function independently in maintaining the non-saponifiable material in solution in the bile or whether they act in combination with the bile acids, as suggested by Wieland and Sorge and Verzár, cannot at present be determined. However, more attention should be given the role of the fatty acids in the production of gallstones.

## Archives of Pathology, Chicago

26: 765-922 (Oct.) 1938

Cerebral Lesions in Hypoglycemia: II. Some Possibilities of Irrevocable Damage from Insulin Shock. A. B. Baker, Minneapolis.—p. 765.
Experimental Production of Tumors in the Brains of White Rats. A. Weil, Chicago.—p. 777.
Medulloblasts of the Infant Brain. C. R. Tuthill, Staten Island, N. Y.—p. 791.
Cytologic Changes in Skin of Mice During Application of Carcinogenic Agents. R. C. Page, Rochester, Minn.—p. 800.
Latent Period in Growth of Spontaneous Mammary Carcinoma in Female Mice of the A Strain. L. C. Strong, New Haven, Conn.—p. 814.
Cardiovascular and Other Lesions in Calves Fed Diets Low in Magnesium. L. A. Moore, E. T. Hallman and L. B. Sholl, East Lansing, Mich.—p. 820.
*Frequency with Which Syphilitic Lesions Are Encountered in Postmortem Examinations. E. T. Bell, Minneapolis.—p. 839.
Pigmented Adenoma of Adrenal. Margaret R. Baker, Akron, Ohio.—p. 845.
Major Duodenal Papilla: Variations of Pathologic Interest and Lesions of Mucosa. A. H. Baggenstoss, Rochester, Minn.—p. 853.

**Frequency of Syphilitic Lesions in Postmortem Examinations.**—Bell in a survey of 27,872 postmortem examinations found definite syphilitic lesions in 2.77 per cent, and in approximately 2.5 per cent syphilis was shown to be the major cause of death. About 3.38 per cent of stillborn infants were syphilitic, and congenital syphilis caused about 2.63 per cent of the deaths in infants less than 1 year of age. Congenital syphilis was a rare cause of death in infants more than 1 year of age. Syphilis was an infrequent cause of death in persons dying in the second and third decades of life. The maximal mortality from this cause occurred in persons in the fourth, fifth and sixth decades of life. Acquired syphilis, in its lethal forms at least, was about twice as frequent in men as in women. The major forms of lethal syphilis were syphilitic aortitis and neurosyphilis, and the age distribution peaks of these two forms were at 45 and 35 years of age, respectively.

## Arkansas Medical Society Journal, Fort Smith

35: 89-104 (Oct.) 1938

Possibilities of Modern Chest Surgery. J. K. Donaldson, Little Rock.—p. 89.
Hyperparathyroidism: Case Report. W. F. Adams, Fort Smith.—p. 92.
Medical Care Plans. R. G. Leland, Chicago.—p. 96.

## Endocrinology, Los Angeles

22: 263-392 (Sept.) 1938

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Changes in Hypophysis and Ovaries of Rats Chronically Treated with an Anterior Pituitary Extract. J. B. Collip, H. Selye and J. E. Williamson, Montreal.—p. 279.
Hormone Studies with Ultracentrifuge: II. Concentration of Anterior Lobe and Pituitary-like Hormones with Ultracentrifuge. Aura E. Severinghaus, L. Levin and J. A. Chiles Jr., New York.—p. 285.
Effect of Hypophysectomy on Restoration of Liver Following Partial Hepatectomy in Rats. C. C. Franseen, A. M. Brues and R. L. Richards, Boston.—p. 292.
Reliability of Present Methods for Characterizing Two Gonadotropic Hormones, Follicle Stimulator and Luteinizer. F. J. Saunders and H. H. Cole, Davis, Calif.—p. 302.
Diabetic Traits in Strain of Rats. Veras V. Cole and B. K. Harned, Philadelphia.—p. 318.
Endocrine Factors Influencing Tumor Development: Effect of Prolan on Marsh-Buffalo Adenocarcinoma. F. Bischoff and M. Louisa Long, Santa Barbara, Calif.—p. 327.
Blood Potassium and Suprarenal Glands. A. D. Marenzi, Buenos Aires, Argentina.—p. 330.
Effect of Testosterone Propionate on X Zone of Mouse Adrenal. W. F. Starkey and E. C. H. Schmidt Jr., Pittsburgh.—p. 339.
Effects of Certain Gonad and Gonadotropic Hormones on Gestation Period of the Rat. C. A. Bunde, Madison, Wis.—p. 345.
Induction of Brooding Behavior in the Jewel Fish. G. K. Noble, K. F. Kumpf and V. N. Billings, New York.—p. 353.

## Indiana State Medical Assn. Journal, Indianapolis

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Causes of Blindness Among the Children at the Indiana State School for the Blind. R. Masters, Indianapolis.—p. 537.
The State and the Blind. Jean R. Kettler and J. M. McCaslin, Indianapolis.—p. 539.
Causes of Blindness in Adults. C. W. Rutherford, Indianapolis.—Blindness in Adults Due to Injury. C. P. Clark, Indianapolis.—p. 547.
Common Causes of Eye Injuries in Children: Ways to Avoid Them. H. Row, Indianapolis.—p. 549.
Conservation of Vision. J. V. Cassady, South Bend.—p. 552.
A Fracture Traction Apparatus for the General Practitioner. W. M. Loehr, Versailles.—p. 554.
Electrosurgical Excisional Biopsy. E. N. Kime, Indianapolis.—p. 556.
A Suggested Plan for Consideration on the Problem of Health Security. N. K. Forster, Hammond.—p. 560.
Foreign Body in the Vagina: Case Report. E. T. Leslie, Evansville.—p. 564.

## Journal of Allergy, St. Louis

9: 535-650 (Sept.) 1938

*Specific Diagnosis and Treatment of Poison Ivy (Rhus Toxicodendron) Dermatitis. A. H. W. Caulfeild, Toronto.—p. 535.
Active Immunization of Allergic Individuals Against Tetanus by Means of Tetanus Toxoid, Alum Precipitated Refined. H. Gold, Chester, Pa.—p. 545.
*Total, Free and Ester Cholesterol Content of Serum in Hay Fever and in Asthma. M. Bruger, F. E. Sammis, W. C. Spain and S. Member, New York.—p. 551.
Tobacco Allergy and Thrombo-Angiitis Obliterans. F. H. Westcott and I. S. Wright, New York.—p. 555.
Emotional Component of Bronchial Asthma. C. H. Eyermann, St. Louis.—p. 565.
Intrapulmonary Inhalation of Benzedrine: Preliminary Report of Some Clinical Effects. O. Swineford Jr., University, Va.—p. 572.
Urticaria of Bacterial Origin. O. C. Hansen-Pruss, Durham, N. C.—p. 577.
Urticaria of Serum Sickness Type: Report of Five Cases. G. L. Waldbott and M. S. Ascher, Detroit.—p. 584.
Retention of Lipiodol in Lungs: Two Case Reports. G. Flamm, New York.—p. 593.
Soybean Sensitivity: Case Report. H. B. Wightman, New Rochelle, N. Y.—p. 601.
Asthma Due to Sensitization to a Mushroom Fly (Aphiochaeta Agarici). R. A. Kern, Philadelphia.—p. 604.
Beet Pollen and Beet Seed Dust Causing Hay Fever and Asthma. L. O. Dutton, El Paso, Texas.—p. 607.
Sensitization to Jute. F. A. Stevens and L. Jordani, New York.—p. 610.

**Poison Ivy Dermatitis.**—The extract from the poison ivy plant that Caulfeild has termed "rholigen," suitably diluted for patch testing, has been found of value in the differential diagnosis of dermatitis regarded as possibly due to contact with poison ivy. The intramuscular injection of this extract in increasing amounts actively influences the severity and duration of an attack of poison ivy dermatitis. Following an adequate series of intramuscular injections of this extract, twenty-three persons susceptible to poison ivy dermatitis have shown a greatly reduced (with a questionable reservation in one case) or even a negative quantitative patch test. Practical clinical results, based on reexposure to the same environment, have confirmed the theoretical conclusion that a satisfactorily reduced quantitative patch test coincides with clinical immunity to ordinary contact with this plant. Dosage and reactions are reciprocal; the greater the degree of sensitivity, the greater the number of injections (from eight to twenty-six injections have been given) which must be given if one is to avoid uncomfortable reactions. The most frequently encountered reaction has been a dermatitis about the site of the injection. At least forty-six persons have been patch tested with rholigen. Twenty-five of these patients were referred with the diagnosis of poison ivy dermatitis. Nine of these gave either a 2, 3 or 4 plus reaction, thus fully confirming the causation. In seven the patch test was negative. With these seven there would seem to be no doubt that the dermatitis was not caused by poison ivy. In the remaining nine cases a 1 plus reaction was obtained. In seven of these the attack was relatively mild and of short duration, so that the clinical diagnosis would seem to be in accord with the results of the tests.

**Serum Cholesterol in Hay Fever and Asthma.**—Bruger and his co-workers determined the cholesterol partition of the serum before and during treatment of 121 patients when they were free from typical attacks of bronchial asthma and seasonal hay fever. The average total cholesterol for the forty-nine patients with hay fever who were treated was 222 ± 67 mg. per

hundred cubic centimeters of serum as compared to the values observed by Sperry in normal adults of 210 ± 50 mg. The average amount of free cholesterol in total cholesterol was 34 ± 8.3 mg. per hundred cubic centimeters, which is somewhat higher than the average normal values. In the treated asthma group (fifty patients) the average total cholesterol was 199 ± 50 mg. per hundred cubic centimeters; the average amount of free cholesterol in total cholesterol was 32.4 ± 7.5 mg. per hundred cubic centimeters. Here again the proportion of free in total cholesterol was somewhat higher than the normal values. In the twenty-two patients with untreated hay fever and asthma (eleven in each group) the average total cholesterol was 198 and 197 mg., and the average free cholesterol in total cholesterol was 29 and 31 mg., respectively. The degree of variation from the treated allergic groups is not noteworthy. Although the average total cholesterol in the treated hay fever group is greater than the average normal figure and in the treated asthma group somewhat lower, the variation from normal is not striking, lacking significance from a statistical point of view.

## Journal of Lab. and Clinical Medicine, St. Louis

**23**: 1223-1332 (Sept.) 1938

Salmonella Suipestifer Infection: Report of Case. D. B. Cole and W. L. Nalle, Richmond, Va.—p. 1223.
*Ascorbic Acid in Blood and Urine After Intravenous Injection of Sodium Ascorbate: Clinical Test for Determining Vitamin C Deficiency. E. S. G. Barron, H. J. Brumm and G. F. Dick, Chicago.—p. 1226.
Notes on Nature and Uses of Protamines in Treatment of Diabetes: Experimental Study of Effect of Protamine Insulinate on Estrous Cycle of White Rats. J. R. Williams, Rochester, N. Y.—p. 1237.
Experimental and Clinical Considerations of Actions of Camphortetrazol, Metrazol and of Schizophrenic Psychoses. D. E. Jackson and Helen L. Jackson, Cincinnati.—p. 1240.
Biochemical and Morphologic Methods for Isolation and Identification of Yeastlike Fungi. C. C. Croft and L. A. Black, College Park, Md.—p. 1248.
*Yeastlike Fungi Isolated from Normal Skins. C. C. Croft and L. A. Black, College Park, Md.—p. 1259.
Glutathione Content of Blood During the Puerperium. J. F. Cadden, New York.—p. 1266.
Determination of Para-Aminobenzenesulfonamide: Micromethod. E. A. MacLachlan, B. W. Carey Jr. and A. M. Butler, Boston.—p. 1271.
Observations on Neufeld Reaction (Quellung Test) Following Desiccation of Pneumococcus Preparations. H. R. Brown, Rochester, N. Y.—p. 1277.
Errors in Erythrocyte Counts Due to Hayem's Solution, Avoided with Gowers' Solution. Y. C. Ch'u, Shanghai, China, and C. E. Forbner, New York.—p. 1282.
Note on Preparation of Urease Reagent for Wrenn's Method for Determination of Urea in Blood and Urine. D. B. Sabine, Yonkers, N. Y.—p. 1296.
Lantern Slides of Photomicrographs in Color: Simplified Method. W. R. Jones, Seattle.—p. 1297.
Simplified Method for Making Photographic Records of Petri Dish Cultures Without Camera. E. Maier, Venice, Fla.—p. 1299.
Method for Protection of Microscopic Mounts for Mailing. H. P. Barret and Theresa Culp, Charlotte, N. C.—p. 1300.
Improved Method of Examination of Spinal Fluid for Diagnosis of General Paresis. H. Hecht, Prague, Czechoslovakia.—p. 1301.
Microchemical Method for Determination of Manganese by Oxidation with Potassium Persulfate: Critical Study of Persulfate Method. T. W. Ray, Milwaukee.—p. 1304.
The Kahn Reactions of Sixty-Four Tularemia Patients. Elizabeth C. Brown and N. Nagle, St. Louis.—p. 1310.

**Ascorbic Acid in Blood and Urine.**—Barron and his associates determined the rate of disappearance from the blood and the urinary excretion of ascorbic acid after the injection of 10 mg. of sodium ascorbate per kilogram of body weight in sixty-three patients. The ascorbic acid content of the blood was estimated by centrifuging oxalated blood in a cold room (3 C.); 2 cc. of the plasma is added to a centrifuge tube containing 6 cc. of trichloroacetic-metaphosphoric acid mixture (1.2 Gm. of metaphosphoric acid ground in a mortar immediately before being dissolved in 40 cc. of a solution of 12.5 Gm. per cent of trichloroacetic acid), shaken together and centrifuged. The supernatant fluid (3 cc.) is titrated with the dilute dye (2 cc. of stock dye [25 mg. of 2,6-dichlorophenol indophenol dissolved in 50 cc. of warm distilled water and filtered] diluted to 25 cc. with distilled water) until a pink color, stable for half a minute, appears. In the urine specimens the ascorbic acid is titrated with the stock dye after the addition of 4 drops of the trichloroacetic-metaphosphoric acid mixture. For the twenty-four hour sample as well as the control twenty-four hour period sample the urine is collected in a bottle containing 25 cc. of five times normal sulfuric acid plus about 50 mg. of 8-hydroxyquinoline and kept in the ice box until the moment of the titration. The "three hour" and "eight hour" samples were titrated after acidification as soon as received. If toluene is added the urine may be kept for twenty-four hours at room temperature with no loss of ascorbic acid. There seems to be, in general, a relation between the content of ascorbic acid in the blood before the injection of ascorbic acid and the percentage of urinary excretion twenty-four hours after the injection; a urinary excretion of ascorbic acid of 10 per cent or less in twenty-four hours is evidence of vitamin C deficiency. Patients having less than 0.4 mg. of ascorbic acid per hundred cubic centimeters of blood showed, as a rule, a low rate of urinary excretion. Contrary to published reports there was no correlation between the content of ascorbic acid in the blood and the rate of its disappearance from the blood after the injection. A survey of the physiologic functions of ascorbic acid suggests that its deficiency may produce varied pathologic alterations other than scurvy. There were three patients with a high ascorbic acid content in the blood and a low urinary excretion. All of them had renal impairment. In the first case the ascorbic acid content of the blood was 2.09 mg. per hundred cubic centimeters and the urinary excretion only 47.4 per cent. In the second case the blood ascorbic acid was 1.75 mg. with a urinary excretion of 13.8 per cent; the patient had an arteriosclerotic cardiac disease associated with cardiac hypertrophy. The third case, with a blood ascorbic acid of 1.32 mg. and a urinary excretion of 18.2 per cent, was that of an adrenal tumor. If ascorbic acid deficiency is observed in Addison's disease (two cases cited) it must be a consequence of low vitamin intake or impaired renal function. It is quite possible that many symptoms observed in gastrointestinal disorders and designated as functional or neurotic are the consequence of hypovitaminosis due to the use of diets poor in vitamin content.

**Yeastlike Fungi from Normal Skins.**—From scrapings from the finger tips and nails of 100 persons, Croft and Black isolated twenty-nine cultures of yeastlike fungi from twenty-two of the persons tested. Persons whose hands were kept moist a large part of the time (kitchen workers, laboratory apparatus washers and housewives) showed a higher incidence to yeastlike fungi than those with drier hands. Twelve cultures were classified as being similar or closely related to Monilia parapsilosis, three as Monilia nigra and three an unidentified Monilia species. Four Endomyces species were isolated. These are the first organisms of this type known to be reported from normal skin. Two Cryptococcus species, one Mycoderma species, one Schizosaccharomyces hominis and three yeastlike fungi that could not be identified were also isolated. Monilia albicans, or any known pathogenic yeastlike fungus, was not isolated from the normal skins.

## Journal of Pharmacology & Exper. Therap., Baltimore

**64**: 1-130 (Sept.) 1938

Pharmacologic Studies on Diothane Hydrochloride. T. H. Rider with E. S. Cook, Cincinnati.—p. 1.
Therapeutic Assay of Neoarsphenamine with Trypanosoma Equiperdum. C. A. Morrell, C. W. Chapman and M. G. Allmark, Ottawa, Ont.—p. 14.
*Effect of Sodium Amytal, Sodium Barbital and Nembutal on Electrocardiogram. Roberts Hafkesbring and Winona MacCalmont, Philadelphia.—p. 43.
Hypnotic Action of Certain Tertiary Butyl Aliphatic Amides. A. D. Bass, Nashville, Tenn.—p. 50.
Placental Transmission of Selenium. B. B. Westfall, E. F. Stohlman and M. I. Smith, Washington, D. C.—p. 55.
Bronchodilator Action of Magnesium and Its Antagonistic Action (Dilator Action) Against Pilocarpine, Histamine and Barium Chloride. V. G. Haury, Philadelphia.—p. 58.
Studies on Native Glucosides of Digitalis Lanata, with Particular Reference to Their Effects on Cardiac Efficiency and Their Toxicity. G. K. Moe and M. B. Visscher, Minneapolis.—p. 65.
Electrocardiographic and Blood Pressure Changes Induced by Posterior Pituitary Extract (Postlobin V), and Influence of Ephedrine Thereupon. K. I. Melville, Montreal.—p. 86.
Anesthesia and Liver Damage: II. Effect of Anesthesia on Blood Sugar, Liver Glycogen and Liver Fat. I. S. Ravdin, H. M. Vars, S. Goldschmidt and L. E. Klingensmith, Philadelphia.—p. 111.

**Effect of Barbiturates on Electrocardiogram.**—Hafkesbring and MacCalmont studied the effect of derivatives of barbituric acid on the electrocardiograms of dogs and cats before, during and after the administration of the drug. The only

cardiac effects of anesthetic doses of barbital, amytal and pentobarbital sodium were an increase in heart rate and a decrease in sinus arrhythmia. Electrocardiograms taken the day after the administration of these drugs showed complete recovery. There was no evidence to indicate the occurrence of cumulative effects or the development of a tolerance to the drugs used.

## Kansas Medical Society Journal, Topeka

**39:** 369-412 (Sept.) 1938

Primary Carcinoma of the Lung: Clinical Study of 160 Cases in Five Years. A. Arkin, Chicago.—p. 369.
Congenital Syphilis. D. N. Medearis, Kansas City.—p. 372.
Negative Phase of Typhoid Vaccination. M. Gerundo, Topeka.—p. 376.
Bilateral Streptococcic Empyema. G. B. Kent and K. C. Sawyer, Denver.—p. 379.
Postoperative Fecal Fistula: Report of Case. M. A. Walker and H. H. Hesser, Kansas City.—p. 382.
X-Ray Treatment of Erysipeloid. M. A. Walker and L. G. Allen, Kansas City.—p. 383.
Use of Barbiturates in Surgery: II. M. A. Walker, G. R. Peters and P. E. Hiebert, Kansas City.—p. 383.

## Missouri State Medical Assn. Journal, St. Louis

**35:** 385-422 (Oct.) 1938

Obesity in the Adult. A. A. Werner and D. C. Weir, St. Louis.—p. 385.
Intermenstrual Pain. D. L. Sexton, St. Louis.—p. 388.
Fat Embolism. A. Sophian and F. H. Scharles, Kansas City.—p. 391.
Treatment of Acidosis in Renal Insufficiency. R. Deakin, St. Louis.—p. 394.
Undulant Fever. H. G. Newman, St. Louis.—p. 398.
Practical Methods of Case Finding. R. H. Runde, Mount Vernon.—p. 403.
Superior Pulmonary Sulcus Tumor Syndrome: Case Report. J. J. Gitt and E. H. Trowbridge Jr., St. Louis.—p. 405.

## New England Journal of Medicine, Boston

**219:** 411-456 (Sept. 22) 1938

Human Encephalitis Caused by Virus of the Eastern Variety of Equine Encephalomyelitis. L. D. Fothergill, J. H. Dingle, S. Farber and M. L. Connerley, Boston.—p. 411.
The Role of Rest and Exercise in Congestive Heart Failure: A Program for Treatment. D. Davis, Boston.—p. 412.
Two Years of Diabetic Surgery. B. Rabinovitz and J. Weisman, Springfield, Mass.—p. 423.
Ragweed-Pollen Survey in Maine for 1937. C. B. Sylvester, Portland, Maine, and O. C. Durham, North Chicago, Ill.—p. 428.
Diverticulum and Sarcoma of Duodenum: Report of Case. A. J. Mendillo and W. B. Kaufman, New Haven, Conn.—p. 432.
Progress in Dermatology. J. L. Grund, Boston.—p. 434.

**219:** 457-502 (Sept. 29) 1938

Trauma Incident to Sports and Recreation. A. Thorndike Jr., Boston.—p. 457.
*Quantitative Differences in Effects of Alcoholic Beverages. H. W. Haggard, L. A. Greenberg and L. H. Cohen, New Haven, Conn.—p. 466.
Study of Seventy-Five Transfusions with Placental Blood. B. C. Grodberg and E. L. Carey, Boston.—p. 471.
The Relief of Chronic Backache and Sciatica by Minor Surgical Measures. W. A. Steel, Philadelphia.—p. 474.
Pneumococcic Pneumonia. F. T. Lord, Boston.—p. 483.

**Effects of Alcoholic Beverages.**—Haggard and his colleagues summarize the usefulness of blood tests for intoxication as follows: (1) demonstration that the blood contains no alcohol is absolute proof of nonintoxication, (2) the finding of alcohol in the blood demonstrates that alcohol has been consumed and (3) more than 1.5 mg. of alcohol per cubic centimeter of blood indicates definite intoxication. They performed numerous experiments on five young men ranging in weight from 150 to 175 pounds (68 to 79.5 Kg.). They were all moderate, occasional users of alcohol. On an empty stomach 63 cc. of 87 proof gin (containing 27.5 cc. of pure alcohol) induced a maximal blood concentration of alcohol of 0.54 mg. per cubic centimeter, while 126 cc. of gin induced a concentration of 1.01 mg. For 90 proof whisky the values for 61 cc. (27.5 cc. of pure alcohol) and 122 cc. were 0.51 and 0.89 mg. respectively. With an increase in the amount of spirit taken the alcohol in the blood does not rise proportionately. The relation is closer for gin than for whisky. Dilution lessens to some extent the concentrations of alcohol reached in the blood. A maximal concentration in the blood of 1.01 mg. was obtained when 126 cc. of straight gin was ingested on an empty stomach, while the same amount diluted to 1,000 cc. with water gave a maximum of 0.92 mg. Under the same circumstances the same amounts of alcohol as whisky gave maximal values of 0.89 and 0.72 mg. respectively. While gin is absorbed more rapidly, it is also eliminated more rapidly. After drinking 55 cc. of alcohol as gin, the alcohol in the blood rose to 1.01 mg. per cubic centimeter but fell to 0.5 mg. in 105 minutes; after drinking the same amount of alcohol as whisky, the alcohol in the blood rose to only 0.89 mg. but did not fall to 0.5 mg. until 135 minutes later. Food in the stomach (within one hour after a breakfast of average size) greatly influenced the rate of absorption and consequently the maximal concentration of alcohol reached in the blood. The maximal concentrations induced by 126 cc. of 87 proof whisky were 0.89 mg. before a meal and 0.35 mg. after one; for the same amount of alcohol as gin the corresponding values were 1.01 and 0.41 mg. A few experiments with meals high in butter, olive oil and milk gave somewhat lower figures than for an average meal, but the results were not strikingly different. Alcohol, when taken as beer, is absorbed much more slowly than when taken as spirit—or even as diluted spirit—and the maximal concentration reached after a given amount of alcohol is lower. Thus while 55 cc. of alcohol as gin gave a maximal blood-alcohol concentration of 1.01 mg. and as whisky 0.89 mg., the same amount as beer (1,222 cc. of 4.5 per cent alcohol by volume) gave a concentration of only 0.44 mg. After a meal the maximum reached for the same amount of beer was 0.24 mg. The rate of absorption varies for the three beverages studied with the amount of buffer substances they contain. A trace of acid is sufficient to render gin acid; whisky requires somewhat more; for beer a considerable amount must be used. These differences suggest that the rate of absorption is influenced by the rate at which the beverage is passed into the intestine. The maximal concentrations in the blood would presumably be correspondingly increased or decreased for persons weighing much more or less than the authors' subjects.

## Philippine Islands Med. Association Journal, Manila

**18:** 481-548 (Aug.) 1938

Studies on Vitamin C: II. Determination of Vitamin C (Ascorbic Acid) in Philippine Vegetables by the Dye Method I. Concepcion, with technical assistance of Maria Luisa Gargaritano, Manila.—p. 481.
Respiratory Data Among Filipinos. N. Cordero, Manila.—p. 491.
Conservative Treatment of Eclampsia. Honoria Acosta-Sison and J. Villanueva, Manila.—p. 497.
Social Justice—and Our Injured Laborers. J. Santillan, Manila.—p. 501.
Preliminary Report on Ileocolostomy. J. Eduque and A. Tangco, Manila.—p. 507.

## Public Health Reports, Washington, D. C.

**53:** 1635-1684 (Sept. 16) 1938

*Incidence of Rheumatic Heart Disease Among College Students in the United States: Based on Replies to a Questionnaire. O. F. Hedley.—p. 1635.
Susceptibility of Mice to Spontaneous, Induced and Transplantable Tumors: Comparative Study of Eight Strains. H. B. Andervont.—p. 1647.
Incidence of Induced Subcutaneous and Pulmonary Tumors and Spontaneous Mammary Tumors in Hybrid Mice. H. B. Andervont.—p. 1665.

**53:** 1685-1732 (Sept. 23) 1938

Studies on Dental Caries: VII. Sex Differences in Dental Caries Experience of Elementary School Children. H. Klein and C. E. Palmer.—p. 1685.
Studies of Sewage Purification: VII. Biochemical Oxidation by Activated Sludge. C. C. Ruchhoft, P. D. McNamee and C. T. Butterfield.—p. 1690.

**Rheumatic Cardiac Disease in College Students.**—Based on 104,163 student health examinations (from eighty-six colleges and universities) Hedley reports an incidence of rheumatic cardiac disease among men students of 9.5 per thousand, while that among women students was 14.9. In fifty-nine coeducational institutions the rate among 53,068 physical examinations on men students was 9 per thousand, while among 27,311 female students it was 11.9. In twenty-nine of these institutions the rate reported was higher among men students and in twenty-eight it was higher among women students, while in two the rates were practically the same. The incidence among 32,863 male students in the fourteen large universities with affiliated medical schools was 6 per thousand, while among 13,235 women students it was 7.4. In one large university, probably owing to some local condition, the rate among women students was

nearly 21. When this university is excluded, the rate among men students is 6.3 per thousand while that among women students is 6. It is extremely doubtful whether sex plays an important part in the incidence of rheumatic heart disease among college students.

## South Carolina Medical Assn. Journal, Greenville

34: 201-226 (Aug.) 1938

Prostatoseminal Vesiculitis. H. Y. Harper, Anderson.—p. 201.
Blood Transfusion: Review of 1,000 Cases. G. R. Dawson, Charleston.—p. 207.

34: 227-250 (Sept.) 1938

Management of Complicated Labor in the Home. R. Torpin, Augusta, Ga.—p. 227.
Use of Hydrogen Peroxide as Diagnostic and Prognostic Test in Vaginitis. G. McCutchen, Columbia.—p. 230.
Growth of Tubercle Bacillus: Restraining or Inhibiting Effect of Carbon Dioxide: Case Report. W. T. Lander, Williamston.—p. 236.

## Surgery, St. Louis

4: 321-482 (Sept.) 1938

Technic of Nailing of Fractures of Neck of Femur. C. Semb, Oslo, Norway.—p. 321.
Relief of Paroxysmal Hypertension by Excision of Pheochromocytoma. A. Brunschwig, Eleanor Humphreys and N. Roome, Chicago.—p. 361.
Malignant Perineal Tumor Simulating Inflammatory Lesions: Two Cases. R. M. Hosler and J. A. Murphy, Cleveland.—p. 371.
Congenital Anorchia: Report of Six Probable Cases of Monorchia. C. E. Rea, Minneapolis.—p. 376.
Torsion of Uterine Adnexa. E. A. Fichlen, New Orleans.—p. 384.
*Cause of Death in Bile Peritonitis. M. H. Manson, New York, and C. T. Eginton, Minneapolis.—p. 392.
Subphrenic Abscess: Medical Review. W. A. Doidge and W. P. Warner, Toronto.—p. 405.
Palmar Fascia in Connection with Dupuytren's Contracture. E. B. Kaplan, New York.—p. 415.
Mixed Tumor of Parotid Gland with Metastasis: Case Report. W. P. Montanus, Cincinnati.—p. 423.
Lipiodol in Treatment of Persistent Fecal Fistula After Appendectomy. S. N. Mendelsohn and L. H. Schriver, Cincinnati.—p. 430.
Unusual Complication Following Suboccipital Craniectomy. M. W. Thorner and R. A. Groff, Philadelphia.—p. 434.

**Cause of Death in Bile Peritonitis.**—In order to demonstrate the noxiousness of intraperitoneal sterile bile and to determine the cause of death in choleperitoneum, Manson and Eginton subjected dogs and guinea pigs to procedures designed to imitate as closely as possible the circumstances under which the condition occurs clinically. From their experiments they conclude that there are at least two factors causing death in choleperitoneum: the primary injury to the peritoneum by the toxic bile salts and the secondary shock from the loss of fluid from the vascular system. The toxic effect of absorbed bile and the bacterial factor may be of importance but, if so, they are probably only contributory to the fatal outcome.

## Tennessee State Medical Assn. Journal, Nashville

31: 337-380 (Sept.) 1938

Perforation of Intestines. E. D. Mitchell Jr., Memphis.—p. 337.
Maneuvers in Abnormal Second Stage of Labor. W. G. Rhea, Paris.—p. 344.
Treatment of Lobar Pneumonia. H. B. Gotten and R. E. Ching, Memphis.—p. 349.
Black Widow Spider Bites. H. T. Kirby-Smith, Winchester.—p. 357.
Treatment of Empyema: Tidal Irrigation. G. H. Kistler, Chattanooga.—p. 362.

## Texas State Journal of Medicine, Fort Worth

34: 257-322 (Aug.) 1938

Cause and Treatment of Functional Uterine Bleeding. E. Novak, Baltimore.—p. 263.
Discussion of Obstetric Anesthesia and Analgesia Based on 5,000 Cases. E. D. Embree, Houston.—p. 268.
Gas Gangrene. R. J. White, Fort Worth.—p. 271.
New Surgical Procedure in Acute Infectious Arthritis: Preliminary Report. H. E. Hipps, Marlin.—p. 276.
End Result in 1,000 Consecutive Industrial Fractures. H. Poyner, Houston.—p. 284.
Radiation Therapy of Fungous Infections. D. Spengler, Dallas.—p. 289.
Study of the Incidence of Intestinal Parasites in 2,800 Persons in Dallas, Texas and Vicinity. H. E. Wright and W. H. Moursund Sr., Dallas.—p. 292.
Gastric Lesion Produced by Posterior Pituitary Extract. M. H. Metz, Dallas.—p. 295.
Management of Heterophoria. C. R. Hartsook, Wichita Falls.—p. 298.
Modern Immunization Program for Children. J. P. Gibson, Abilene.—p. 301.
Study of Morphine, Scopolamine and Atropine and Their Relation to Preoperative Medication and Pain Relief. R. M. Waters, Madison, Wis.—p. 304.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

## Archives of Disease in Childhood, London

13: 193-288 (Sept.) 1938

Wilms' Embryoma: Clinicopathologic Study. Ruby O. Stern and G. H. Newns.—p. 193.
*Esophagitis in Infancy. J. H. Ebbs.—p. 211.
Symmetric Degeneration of Neostriatum in Chinese Infants. W. J. C. Verhaart.—p. 225.
Clinical Ascariasis in Children. Cicely D. Williams.—p. 235.
Precocious Puberty: Report on Case of Pineal Syndrome. A. V. Neale.—p. 241.
Congenital Pyloric Stenosis in First and Second Cousins. E. A. Cockayne.—p. 249.
Nutritional Edema in Children in Egypt. H. Shukry, M. A. Mahdi and A. A. El Gholmy.—p. 254.
*Spontaneous Subarachnoid Hemorrhage in Children: Clinical Study of Five Cases. H. G. Miller.—p. 258.
Congenital Hemolytic Anemia with Normal Fragility of Red Blood Cells. E. Schiff.—p. 264.

**Esophagitis in Infancy.**—In a review of the records of the Birmingham Children's Hospital for the last three years, Ebbs found that, whereas thirty-one children have been admitted for treatment of foreign bodies in the esophagus, poisoning and congenital strictures, twenty-eight children have died with an acute esophagitis. The age of the former group was between 1 and 12 years and those with acute esophagitis were less than 10 months of age, the average being 4 months. Thrush was the etiologic factor in twenty-two cases, diphtheria in two, tuberculosis and Vincent's organism in one each, and in three there was ulceration and inflammation of the esophagus without a specific organism being demonstrated.

**Spontaneous Subarachnoid Hemorrhage in Children.**—Five cases of spontaneous subarachnoid hemorrhage are reported. Although neither of the two fatal cases came to necropsy, Miller states that the diagnosis in every instance was confirmed by examination of the cerebrospinal fluid. The clinical picture in all five cases was so strikingly similar to that known to occur in adults that in the three cases in which there were no complicating factors similar pathologic changes are suspected. Intracranial aneurysm of the type that gives rise to subarachnoid hemorrhage in the healthy young adult has not been recorded frequently in children, but if, as structural evidence suggests, these aneurysms are truly congenital in nature, they must obviously be present (perhaps on occasion only) at birth. The frequently reported association between intracranial aneurysm and coarctation of the aorta is further evidence in favor of a congenital origin, and Fearnsides reports one significant case of a definite aneurysm of the circle of Willis found at necropsy in a child of 19 months dying of bronchopneumonia complicating gastritis. It is suggested that in three of the cases the hemorrhage was in all probability due to rupture of a congenital intracranial aneurysm and that pathologically as well as clinically these cases are analogous to spontaneous subarachnoid hemorrhage occurring in adults. One of the other two patients was at stool when the hemorrhage with loss of consciousness occurred, while the other patient had a facial hemangioma, and some similar intracranial pathologic change is suspected as the cause of the hemorrhage. The pyrexial phenomena associated with the hemorrhage were somewhat inconstant as compared with those occurring in adults.

## British Medical Journal, London

2: 555-604 (Sept. 10) 1938

Occipitoposterior Positions of Vertex and Their Complications. C. Mole.—p. 555.
*Interruption of Early Pregnancy by Means of Orally Active Estrogens. A. S. Parkes, E. C. Dodds and E. L. Noble.—p. 557.
Observations on Treatment of Empyema in Children. H. L. Wallace.—p. 560.
Synergy in Experimental Chemotherapy of Staphylococcic Infections. S. P. De and U. P. Basu.—p. 564.
Daylight in Relation to Climate and Health. W. R. G. Atkins.—p. 565.

**Interruption of Early Pregnancy by Estrogens.**—Parkes and his colleagues investigated the capacity of two estrogenic substances (from 0.25 to 1 mg. of ethinyl estradiol and from 1 to 4 mg. of diethyl-stilbestrol), given orally, to suppress the action of progesterone and to prevent pregnancy. The

substances were fed to rabbits in propylene glycol solution, which was swallowed readily. They found that small doses of orally active estrogen will prevent implantation of the blastocyst if given soon (two to seven days) after ovulation or may terminate established pregnancy. The effect is produced in what is essentially a physiologic manner: the luteal phase of the cycle is suppressed and another phase is induced which, though not abnormal in itself, is unsuitable for the development of the embryo. Everything that is known about the menstrual cycle of primates suggests that its hormone control is the same as in lower animals and it is extremely probable that the factors governing the implantation of the fertilized egg are fundamentally similar in women. The conclusions arrived at should thus be applicable to women, though the fact that very large amounts of estrogen are excreted by pregnant women makes it likely that the period during which estrogenic treatment might be effective would be relatively much shorter than in rabbits.

2: 605-644 (Sept. 17) 1938

Vertigo: Its Neurologic, Otologic, Circulatory and Surgical Aspects. W. R. Brain.—p. 605.
Cooperation Between Ophthalmologist and Physician in Certain Cases of Visual Loss. C. B. F. Tivy.—p. 608.
*New Type of "Jacket" Respirator for Treatment of Poliomyelitis. A. F. Burstall.—p. 611.
Diagnosis of Whooping Cough. A. B. Donald.—p. 613.
Human Oil in Treatment of Adherent Scars. C. P. G. Wakeley.—p. 618.

**New Respirator for Poliomyelitis.**—Burstall describes a jacket respirator that consists of an aluminum cuirass made in one piece, which is hammered out to the shape of the thorax. It encloses the trunk of the patient from the neck down to the waistline and is connected to the pulsating apparatus by a 1 inch flexible hose. It can be connected to a respirator of cabinet type. The capacity of a cuirass is so small that a large number of them may be operated from one cabinet type respirator by drilling a hole in the cabinet and connecting a hose to it. Inside the cuirass is a sponge rubber vest, 1 inch thick, with holes for the arms, neck and waist. The openings in the cuirass have a beaded edge and are closed to the body by soft sheet rubber jointing pieces, which are held to the cuirass by being lifted over the beaded edge. Rubber rings may also be added to prevent the sheet from working off the beaded edge. The cuirass is provided with four metal lugs for the attachment of arm splints. The whole of the metal work can be sterilized. It weighs only 6 pounds for a patient 10 years of age. Three sizes of cuirass will provide for patients ranging from the age of 3 years up to medium-sized adults. The time taken for two persons to dress a sick patient completely in the new respirator is seven minutes without splints and from ten to twelve minutes with splints. This respirator is therefore not as suitable for the treatment of emergency cases as respirators of the Drinker type.

## Edinburgh Medical Journal

45: 605-664 (Sept.) 1938

Experimental Neuroses in Animals and Their Treatment with Bromides. B. P. Babkin.—p. 605.
Right-Sided Aortic Arch. J. P. McGibbon.—p. 620.
William Osler. J. Hay.—p. 631.
Pernicious Anemia and Its Treatment. A. Goodall.—p. 648.
Biologic Properties of Killed Tubercle Bacilli Deprived of Acid-Fastness by Method of Browning and Gulbransen. Mary A. Griffin.—p. 654.

## Glasgow Medical Journal

12: 109-172 (Sept.) 1938

Nonsurgical Treatment of Cataract. J. Burdon-Cooper.—p. 109.

## Guy's Hospital Reports, London

88: 257-370 (July) 1938

Arthur Edwin Boycott. G. W. Goodhart.—p. 257.
Studies on Tumor Formation. G. W. Nicholson.—p. 263.
Granulosa Cell Ovarian Tumor as Cause of Sexual Precocity: Report of Case. Min Sein.—p. 299.
Head Noises and Cranial Bruits. W. G. Sears.—p. 308.
Report on Cases of Perineal Swellings Due to Inflammation and Other Causes Occurring in Genito-Urinary Department at Guy's Hospital, 1910 to 1936. A. R. Thompson.—p. 320.
Psychologic Investigation of Case of Dermatitis Artefacta. F. W. Brown.—p. 356.
Importance of Breast Feeding in Prevention of Diarrhea and Vomiting of Infancy. N. M. Jacoby.—p. 367.

## Irish Journal of Medical Science, Dublin

No. 153: 341-596 (Aug.) 1938

Report of the Rotunda Hospital (Nov. 1, 1936, to Oct. 31, 1937). A. H. Davidson, R. C. Sutton and J. B. Fleming, G. Dockeray, C. L. McDonogh and W. R. F. Collis.—p. 341.
Clinical Report of the Coombe Lying-in Hospital, 1937. R. M. Corbet, J. A. Finegan and J. K. Feeney.—p. 438.
Clinical Report of the National Maternity Hospital. J. F. Cunningham, P. J. McMahon and J. Gallagher.—p. 511.
Note on Speculum Matricis of James Wolveridge. T. P. C. Kirkpatrick.—p. 577.
A Visit to the Clinics of Frankfort and Heidelberg. R. M. Corbet.—p. 578.

## Journal of Tropical Medicine and Hygiene, London

41: 261-276 (Aug. 15) 1938

Protective Inoculation Against Typhus. M. A. Gohar.—p. 261.
Fourth Note on Infectivity to Man of Strain of Trypanosoma Rhodesiense. J. F. Corson.—p. 262.
Trypanosomiasis Gambiensis: Some Observations in Uganda and Their Bearing on Prophylaxis. A. A. F. Brown.—p. 265.

## Lancet, London

2: 651-704 (Sept. 17) 1938

*Severe Hemorrhage from Stomach and Duodenum. T. I. Bennett, J. Dow, F. P. L. Lander and S. Wright.—p. 651.
Some Observations on Arches of Foot and Flat Foot. J. Bruce and R. Walmsley.—p. 656.
Coarctation of Aorta: Report of Two Cases. Joan B. Walker and F. D. M. Livingstone.—p. 660.
Fits and Schizophrenia. S. W. Gillman and D. N. Parfitt.—p. 663.
Ketonemia in Diabetes and Pregnancy. C. H. Gray.—p. 665.
Staphylococcic Septicemia Treated with 2-(p-aminobenzenesulfonamido) Pyridine. W. J. Fenton and F. Hodgkiss.—p. 667.
Facial Carbuncle Treated with Prontosil Album: Personal Experience, with Note on Its Effect in Lupus Erythematosus. H. W. Barber.—p. 668.
Immunologic Connection Between Burns and Sepsis. W. H. Hughes.—p. 670.

**Hemorrhage from Stomach and Duodenum.**—Bennett and his colleagues studied 122 cases in which life was endangered by gastric and duodenal hemorrhage. The severity of any case can be judged only when it is known how much blood has been lost and whether bleeding has ceased, temporarily or permanently. Determinations of the volume of blood lost revealed that in thirty-three cases the amount of blood lost did not amount to more than one fifth of the total blood volume, while in thirty-two it was not more than one half. That the estimation of blood volume is a genuine criterion of severity is indicated by the fact that the fatal cases were confined to the group in which the volume of blood was notably reduced (more than 50 per cent). It is to be noted that it is the fraction of the total blood volume consisting of the cells which is the all important one. The total blood volume is also the only certain guide available for the determination of whether actual hemorrhage has ceased or not. In the hours after hemorrhage has begun the hemoglobin percentage must be expected to continue to fall for some time whether the actual hemorrhage has ceased or not. Though it is true that, if hemorrhage is continuing the fall of hemoglobin may be greater than if it has been arrested, this is not necessarily so owing to the variation in the intensity of the bleeding from case to case. The one fact which points inevitably to the conclusion that bleeding is still in progress is that the cell volume has diminished in the second case whereas it remains unchanged in the first.

## Medical Journal of Australia, Sydney

2: 405-446 (Sept. 10) 1938

Diverticulosis and Diverticulitis. C. B. Blackburn.—p. 405.
Diverticulosis and Diverticulitis from Radiologic Point of View. H. R. Sear.—p. 409.
Occurrence of Juxta-Articular Nodules in Australia. F. J. Fenner.—p. 412.
Some Aspects of Psittacosis and Isolation of Virus. A. R. Tremain.—p. 417.
Some Observations on Use of Protamine Zinc Insulin in Management of Diabetes Mellitus. E. Downie.—p. 421.

## South African Medical Journal, Cape Town

12: 569-612 (Aug. 27) 1938

Pancreatitis. A. Radford.—p. 585.
Pellagra. L. R. Brumberg.—p. 587.
Malarial Pyrotherapy for Syphilitic Disease of the Central Nervous System. D. S. Huskisson.—p. 589.
Insulin Therapy. J. A. Higgs.—p. 590.
Colospasm. R. Schaffer.—p. 594.

## Archives des Maladies du Cœur, Paris

32: 765-884 (Aug.) 1938. Partial Index

Experimental Contribution to Physiopathology of Arteriovenous Aneurysm. A. Tournade and E. Curtillet.—p. 766.
Paroxysmal Ventricular Tachycardia in Experimental Auriculoventricular Block. R. Froment and F. Jourdan.—p. 792.
Electrocardiographic Studies in Course of Treatment of Schizophrenia with Metrazol. E. Gérandel.—p. 811.
Cardiac Automatism. E. Donzelot.—p. 817.
*Therapeutic Action of Adenosine. R. Fabre.—p. 824.
Rheumatismal Auriculoventricular Block. C. G. Marchal, J. Lenègre, Busson and Mathivat.—p. 844.

**Therapeutic Action of Adenosine.**—Fabre says that animal experiments with adenosine revealed that this substance has a notable vasodilating effect on the coronary vessels. He regards the hyposensitive effect observed by some as of slight importance, because in his own experiments on dogs he found that the decrease in arterial pressure is of only short duration (a few seconds). Moreover, adenosine seems to have no toxic effect if it is given in suitable doses. On the basis of experimental results and encouraged by the therapeutic effects obtained in human subjects by the oral administration of adenosine, the author decided to try the intramuscular injection in daily doses of from 5 to 10 mg. (2.5 mg. per cubic centimeter of physiologic solution of sodium chloride). He reviews the clinical histories of ten patients with symptoms of angina pectoris in whom he resorted to the intramuscular injection of adenosine. Some of the case histories indicate that he administered 5 mg. at each injection and that the total number of injections varied between six and twelve. In eight of the ten patients the intramuscular injections of adenosine proved effective but in two cases they had no effects on the anginal symptoms. This failure in some cases the author regards as additional proof of the fact that the pathogenic mechanism of the anginal syndrome is not the same in all cases.

## Presse Médicale, Paris

46: 1385-1400 (Sept. 17) 1938

General Review of Influenza: Anti-Influenzal Serum Therapy. A. Béclère.—p. 1385.
*New Method of Treatment for Dermal Leishmaniasis (Oriental Sore). F. Flarer.—p. 1388.

**New Treatment for Dermal Leishmaniasis.**—Dermal leishmaniasis being comparatively frequent in Sicily, and its treatment not being entirely satisfactory as yet, Flarer decided to try the antiprotozoal medicament atabrine, which had been found highly effective not only in the treatment of malaria but also in another protozoal disease, namely lambliasis. The author describes his experiences with this treatment in fourteen cases of dermal leishmaniasis. In the first four cases he combined general and local treatment. The general treatment consisted either in the oral or in the intravenous administration of the medicament. Although it improved the local lesions and reduced the number of protozoans, they did not completely disappear until local treatment was instituted. In the first case, the author says, it was given in the form of intradermal injections so as to soak the entire ulceration with atabrine dissolved in distilled water. The slight edema which followed persisted for about twenty-four hours, but without a trace of inflammatory reaction and without noticeable local pain. The ulceration regressed rapidly and the protozoans disappeared and remained absent after a month of observation, in the course of which the ulceration had been smoothed out. This and three other cases, in which general and local treatment was used, having convinced the author that the local treatment was the more effective, he used local treatment exclusively in the other ten cases of dermal leishmaniasis. In four cases he tried half doses (0.05 Gm. of atabrine) repeated twice at three day intervals. Since the local tolerance was excellent, he later administered 0.1 Gm. of atabrine dissolved in 1 or 2 cc. of distilled water, depending on the size of the ulceration. This treatment was followed by permanent cure with disappearance of the protozoans, even after a single injection. The author concludes that it is unquestionable that this treatment has advantages over all of those hitherto employed.

68: 1401-1416 (Sept. 21) 1938

Vascular Therapy in Aortic Insufficiency and in Mitral Insufficiency. A. Ferrannini.—p. 1401.
Gangrene of Extremities of Venous Origin. M. Audier and H. Halmovici.—p. 1403.
*Role of Vitamin $B_1$ in Humoral Regulation of Nervous System: Therapeutic Suggestions. B. Minz.—p. 1406.

**Vitamin $B_1$ and Nervous System.**—Minz reviews Loewi's theory of the humoral transmission of the nervous impulse which assumes the liberation of two antagonistic substances at the nervous terminations, one of the type of acetylcholine and another of the type of epinephrine. After citing recent investigations on the role of acetylcholine in the excitation of the nerves, he reports some of his own observations which suggested to him that the extract of the nerve that had been subjected to excitation contained, in addition to the substance of the acetylcholine type, a second substance which reinforced the action of the first. Investigations on the nature of this substance disclosed that its action was like that of a ferment. Consequently he searched for a substance with this type of action in yeast, and experience confirmed the supposition that this substance exists in yeast. In view of the fact that yeast is rich in vitamins, particularly the vitamins the deficiency of which produces nervous disturbances, he investigated whether the substance might perhaps be identical with the antineuritic factor, that is, vitamin $B_1$. He was able to show that vitamin $B_1$ is capable of strengthening the effect of acetylcholine and that in the humoral mechanism of nervous excitation vitamin $B_1$ assumes a role of coferment of acetylcholine. He shows that the strengthening of the actions of one of these agents by the other is not only of scientific but also of practical interest. On the one hand it may serve as a basis for the interpretation of the syndrome of $B_1$ avitaminosis and of related conditions; on the other hand it is of value for the therapy of a group of nervous disturbances. The absence of the coferment of the acetylcholinic action explains some symptoms of beriberi such as tachycardia, the disappearance of the patellar and achilles tendon reflexes, the disturbances of coordination, the atrophy of the muscles and the neuritic, paralytic and gastrointestinal disorders. Moreover, it is known that several of these phenomena are present in febrile diseases such as malaria, typhoid, dysentery and pneumonia and even in the banal infections. Finally they are observed in the course of conditions which are accompanied by an augmentation of the metabolism (pregnancy, lactation and physical exertion). It appears that these symptoms are brought on by the factors which increase the organism's need for vitamin $B_1$. Among the agents which disrupt the optimal equilibrium between acetylcholine and vitamin $B_1$ there is, in addition to certain micro-organisms, also the cancerous cell, a fact which is of great importance for the study of cancer. Favorable therapeutic effects of vitamin $B_1$ have been observed in cases of neuritis and even in several cases of multiple sclerosis, also in the nervous symptoms of pernicious anemia. Discussing the latter disease, the author points out that favorable therapeutic results have been obtained with acetylcholine. However, because the action of this substance is of extremely short duration, he thinks that the preliminary administration of vitamin $B_1$ will make the action of acetylcholine more intensive and lasting.

## Schweizerische medizinische Wochenschrift, Basel

68: 1089-1108 (Sept. 24) 1938. Partial Index

Present Status of Research on Hormones in Gynecology. O. Keller.—p. 1089.
*Epidemic Myalgia (Bornholm Disease). E. Jenny.—p. 1092.
Pathogenesis of Pulmonary Collapse by Blockage of Air Passages. Hilde Lachmann-Mosse.—p. 1094.
Investigations on Antigenic Function of Vitamin A. J. P. Kleperzak. p. 1098.

**Epidemic Myalgia.**—Jenny reports the clinical histories of two brothers aged 9 and 8 years. The 9 year old boy became ill with sudden fever and headache. Then he developed severe muscular pains especially in the lower part of the thorax and over the stomach. The pains became exacerbated in successive attacks and were felt especially during deep respiration. The epigastric region was highly sensitive to the touch and the right abdominal rectus seemed slightly swollen. Coughing and other catarrhal symptoms were lacking. There were no pneumonic murmurs or pleuritic rub. Following a temporary sub-

sidence of the pains and fever they recurred once more, but then they subsided again and after six days the boy was well again. Two days after this boy had become ill his younger brother showed the same symptoms. The author had never encountered this disorder but recalled having read about the occurrence of epidemic myalgia in the Scandinavian countries. Reviewing the literature on this disease, he points out that it appears in smaller or larger epidemics, especially during the summer and fall months. It attacks chiefly young persons and children. The incubation period varies between two and four days. Infectiousness has been known to persist for four weeks after the recovery of the patient. The myalgia involves chiefly the intercostal muscles, the diaphragm and the abdominal recti and obliqui. This explains why respiration, particularly the inspiration, is so painful and why the respiration is superficial and accelerated, so that pneumonia or pleurisy may be thought of. The severe muscular pains have been compared with "stitches in the side" and in the popular language they have led to such designations as "lung stitches" or "devil's grip." The involved musculature is sensitive to pressure, but the skin is not hypersensitive. Swelling or hardening of the muscle is observed in some instances. The disease usually persists for eight or ten days. The prognosis is favorable for the myalgia as well as for the complications. The therapy is purely symptomatic. The etiology and pathogenesis are still unknown, but many observers assume that it is a virus disease. Reviewing the geographic distribution of epidemic myalgia, the author points out that since Sylvest's description of an extensive epidemic on the Danish island of Bornholm the disease has been known also under the term of Bornholm's disease. Regarding the probable origin of the cases here described, he says that the father of the boys had attended a course in which sixty-two Danes participated, and inquiry in Denmark disclosed that cases of epidemic myalgia had occurred there during July and August. It is possible that one of the men from Denmark was a virus carrier.

## Annali dell'Istituto "Carlo Forlanini," Rome

2: 437-576 (July-Aug.) 1938. Partial Index

*Influence of Pneumoperitoneum on Electrocardiogram. V. Agnello.—p. 437.
Partial Pneumothorax and Elastic Anterolateral Thoracoplasty. S. Gunella.—p. 445.
Electrocardiographic Researches in Deviation of Mediastinum in Course of Artificial Pneumothorax. V. Agnello.—p. 461.
Pneumoperitoneum in Abdominal Disturbances from Pleurisy. P. Guglielmetti.—p. 489.

**Influence of Pneumoperitoneum on Electrocardiogram.**—Agnello observed the behavior of the electrocardiogram before and after establishment of pneumoperitoneum in twenty patients suffering from tuberculosis. Collapse treatment, especially by artificial pneumothorax, was already established in the majority of the cases. The electrocardiograms were taken of patients at rest and during fasting, immediately before and after an insufflation of about 300 cc. of oxygen into the peritoneal cavity. Pneumoperitoneum induced an increase of the pause between two consecutive cardiac revolutions (atrioventricular complexes), as shown by the prolongation of the TP space in the electrocardiogram and also alterations of the R, S and T waves in the three leads. According to the author the electrocardiographic alterations are due to deviations of the electrical axis from displacement of the heart and also to functional changes of the heart from vagosympathetic stimulation. The functions of the heart are good in pulmonary tuberculosis before and after establishment of collapse of the lung and of pneumoperitoneum. The latter has both a mechanical action and a capacity of stimulating the sympathetic nervous system.

## Minerva Medica, Turin

2: 197-220 (Sept. 1) 1938

Undulant Fever with Hemorrhagic Purpura of Werlhof's Type and Hypoplasic Global Myelosis. O. De-Rin.—p. 197.
*Hydronephrosis and Abnormal Renal Vessel: Clinical Study. L. Annibaldi.—p. 205.

**Hydronephrosis and Abnormal Renal Vessel.**—Annibaldi reports seven cases of hydronephrosis in persons having a vessel of abnormal course. According to the author the ptosis of the kidney, the various congenital malformations existing in cases of abnormal renal vessels and the presence of general or local infection are the main causal factors of hydronephrosis. The pathogenic role of the vessel is of secondary importance. A renal artery, especially a branch of the renal artery or of the aorta, follows an abnormal course more frequently than a renal vein. Generally the vessel follows an oblique downward direction to the lower pole of the kidney and it embraces the ureter either anteriorly or posteriorly. The diagnosis of the condition is made by roentgen examination of the kidney and of the urinary tract and ascending pyelography when hydronephrosis is already established and by pyeloscopy early in the development of pelvic stagnation which precedes hydronephrosis. The treatment is surgical. If the function of the involved kidney is good, conservative treatment is advisable. Otherwise nephrectomy is indicated, especially if the parenchyma of the involved kidney shows grave changes or if there is a renal infection.

## Rivista di Neurologia, Naples

11: 281-376 (Aug.) 1938

*Neurologic Syndromes of Recklinghausen's Neurofibromatosis. F. Vizioli and S. Tolone.—p. 281.
Cerebral Multiple Tumor (Glioblastoma) of Pons and Corpus Callosum Without Psychic Syndromes. D. Alessi.—p. 321.
Spasmodic Scoliosis in Differential Diagnosis Between Symptomatic Lumbar Ischialgia from Compression of Cauda Equina and Idiopathic Lumbar Ischialgia of Long Duration. C. Mazzi.—p. 340.

**Neurofibromatosis.**—Vizioli and Tolone report four cases of diffuse neurofibromatosis of Recklinghausen's type, with important peripheral and central neurologic complications. In the first case the neurologic symptoms were those of an intramedullary tumor at the cervical segment of the spinal cord with formation of intratumoral cavities of the syringomyelic type. The second patient showed cerebral symptoms from bilateral multiple neurofibroma of the posterior cranial fossa (deafness, blindness and disturbances in walking). He had a nodule at the right laterocervical region which for the last few months had been painful on pressure and followed a rapid development. The nodule was removed. It was found that it had been transformed into sarcoma of the neurofibromatous type which does not produce metastases. The third patient had suffered in childhood from a nervous disease (either polyneuritis or poliomyelitis) from which residual left facial paralysis and atrophic paralysis of a leg remained. He showed symptoms of compression of the cervical segment of the spinal cord from an extramedullary tumor which seemed to originate in the distal roots of the right cervical nerves. The fourth patient had a complete spastic paraplegia with contracture in flexion from spinal trauma. The neurologic syndrome consisted in complete flaccid paralysis of the left arm from compression of the brachial plexus by a large fibrosarcoma deeply seated in the axillary cavity. The patient had in association an incomplete acromegalic syndrome. The author made a microscopic study of the tumors removed by operation, of the cutaneous nodules and of some neurofibromas, taken by biopsy in all but the first case, which was the most simple. He found that the skin nodules and an extramedullary tumor had the typical microscopic aspect of neurofibromatosis of Recklinghausen's type. The tumor showed sarcomatous degeneration in two cases. Some oligodendroglia of the first (Robertson) and second types (Cajal) were identified in the preparations of neurofibroma. In connection with the cases reported the author discusses the pathogenesis of neurofibromatosis of Recklinghausen's type, which he believes originates in defective development of the nervous system during embryonal evolution. The endocrine disorders that precede or are associated with the disease are secondary factors.

## Deutsche Zeitschrift für Chirurgie, Berlin

250: 705-756 (Aug. 31) 1938

Nerve Apparatus of Human Lung and Its Clinical Significance. P. Sunder-Plassmann.—p. 705.
*Surgery of Funnel Shaped Chest. H. Krauss.—p. 715.
Contributions to Hemorrhage at Base of Skull. O. Voss.—p. 727.
Cystic Lymphangioma of Small Intestine. V. Priverid.—p. 736.
Tumor of Colon in a Hernial Sac. F. Gerhardt.—p. 742.

**Surgery of Funnel Shaped Chest.**—According to Krauss the congenital type of funnel shaped chest is characterized by the fact that it becomes deeper with the growth of the person

and the transverse diameter of the thorax larger. The deformity is as a rule symmetrical with the deepest point opposite the ninth and tenth thoracic vertebrae. The deformity affects the mediastinal organs and the respiratory movements. The clinical symptoms depend on the depth of the depression and the capacity of the intrathoracic organs to accommodate themselves to the altered mechanical relationship. The majority of the children so afflicted do not present functional disturbances of any kind. In a small proportion of the cases the deformity results in a narrowing of the chest and a marked dislocation of the mediastinal structures. The distance between the posterior wall of the sternum and the vertebral bodies may be shortened by several centimeters. The heart may become displaced to the left and the venae cavae compressed, leading to stasis, distention of the veins of the neck, cyanosis and dyspnea. The more or less fixed thoracic wall interferes with respiratory movements and leads to hypoventilation of pulmonary tissue. Such patients complain of shortness of breath, frequent attacks of bronchitis, palpitation, weakness and early fatigue; difficulty in swallowing and asthmatic attacks may occur. The aim of the operative intervention, according to the author, is the enlargement of the mediastinal space. The loss of the sternum, however, deprives the mediastinal structures of their protection as well as causes the direction in which the ribs move to be altered. In 1931 Sauerbruch and Nissen devised an operation in which the mediastinal space was enlarged by advancing the sternum in line with the thorax. It consisted of linear sectioning and removal of small portions of cartilages from the fourth to the eighth ribs on the left side at one sitting, while at the second sitting wire sutures were introduced through the right side of the sternum and attached to an extension apparatus. In the course of eight days the sternum was advanced so as to arrive at the level of the thorax. Ombrédanne's T shaped osteotomy, while effective, had a high immediate mortality, presumably caused by too sudden alteration in the position of the heart and the large vessels. The danger attendant on all types of operations is tearing of the pleura and subsequent pleural extravasation.

## Münchener medizinische Wochenschrift, Munich

BB: 1337-1376 (Sept. 2) 1938. Partial Index

*Ocular Origin of Migraine in Children and Young Persons. K. Grunert. —p. 1337.
Recognition of Disposition for Cancer: Laboratory Tests for Detection of Disposition. J. Kretz.—p. 1341.
Quinine as Abortifacient. Koopmann.—p. 1344.
Irradiated Fresh Milk for Continuous Feeding. K. Scheer.—p. 1346.
Hypertrophy of Prostate: Diagnosis and Treatment. E. Thiermann. —p. 1347.

**Ocular Origin of Migraine in Children.**—For a period of ten years, Grunert made careful functional tests on the eyes of all patients who were subject to headaches and to migraine and, as far as possible, of the relatives of these patients who were subject to headaches. In the course of these studies he made two significant observations: 1. In the majority of the patients with headaches and in nearly all of those with migraine there existed disturbances in the ocular function. 2. The treatment of these ocular disturbances reduced or completely removed the general symptoms to such an extent that a causal connection could not be denied. In children and young persons the ocular origin of migraine was even more pronounced than it was in adults. The author reports observations in more than 200 cases of migraine in children and young persons. Many of the patients were of the type referred to as "difficult" children; that is, they showed signs of nervous irritability, they were difficult to manage or were inattentive in school and so on. Ocular examination disclosed defective refraction, disturbances in the ocular equilibrium and defects in the accommodation. In many of these children the growth of the eyes is not completed as early as in others and school, requiring a considerable amount of close work, involves a great strain on these still growing eyes. After describing some of the difficulties of these children and of the symptoms likely to develop in them, the author gives his attention to the treatment of the migraine of ocular origin. He emphasizes that even slight optic defects may cause severe subjective disturbances. After the refractive defects have been corrected, close work is avoided for one or two weeks and the weakened muscle of accommodation is treated with pilocarpine. The administration of pilocarpine must be individualized. It is best to administer it in the evening before the patient goes to sleep. In severe cases it can be given also during the day, but in this case the individual doses are, of course, smaller. In case of disturbances in the muscular equilibrium or in latent strabismus, prisms are employed; occasionally an operation for strabismus may be resorted to or stereoscopic exercises may be employed. In the few cases in which no anomalies of refraction exist and in which there is no impairment of the muscular equilibrium, but only an insufficiency of the apparatus of accommodation, the migraine is cured by resting the eyes for a while and by treatment with pilocarpine. The ocular treatment effected cure in 197 children and young persons with migraine. The author closes his report by recommending that all children in whom migraine is suspected be subjected to a thorough examination of the eyes.

## Zeitschrift für Kinderheilkunde, Berlin

60: 77-180 (Aug. 26) 1938. Partial Index

*Development of Bacteria and of Lactic Acid in Milk to Which Citric Acid Has Been Added. W. Goeters.—p. 77.
*Fermentation of Citric Acid by Bacteria. W. Goeters.—p. 87.
*Changes Caused by Citric Acid Milk in Qualitative Composition of Bacterial Flora in Stools of Nurslings. W. Goeters.—p. 92.
Prognosis of Tuberculosis in Nurslings and Small Children. J. Bohlin.—p. 95.
Westphal's Sign in Diseases of Cerebellum. Eleonore von Kirschten. —p. 128.
Method for Counting Thrombocytes in Children. E. Lorenz.—p. 142.
Specific Serotherapy and Malignant Diphtheria. F. Teutleale.—p. 172.

**Bacteria and Lactic Acid in Milk Treated with Citric Acid.**—After pointing out that the various dilutions of milk (half-milk, third-milk and so on) are not only superfluous but may even be harmful in the treatment of nurslings, Goeters says that it has been proved that whole milk which has been treated with lactic acid is superior to all types of diluted milk. He says that the favorable effects obtained with buttermilk in the treatment of dyspeptic nurslings are probably not so much the result of the acidity of this type of milk as of its comparatively high lactic acid content. However, not only lactic acid but other organic acids, particularly citric acid, have been found valuable as additions to whole milk in the feeding of nurslings. Some pediatricians regard citric acid as better for this purpose than lactic acid. After citing some previous studies on citric acid milk and experiences with it, the author describes bacteriologic studies which he himself made on whole milk to which citric acid had been added. He found that this type of milk promotes the growth of the most important lactic acid bacteria (lactic acid streptococci, beta cocci, Bacterium lactis aerogenes) but that it suppresses the development of Bacterium coli, micrococci and tetracoci and that it leaves other types of bacteria (Bacillus proteus and Bacillus subtilis) entirely unchanged. The percentage of lactic acid produced by bacterial action in citric acid milk is such that it exerts a favorable influence on the metabolism of healthy nurslings.

**Fermentation of Citric Acid by Bacteria.**—Goeters investigated whether citric acid serves as a source of carbon for the most important milk or fecal bacteria. He found that in citric acid milk as well as in synthetic nutrient solutions Bacterium lactis aerogenes, beta cocci, Bacillus proteus and B. subtilis and the majority of milk or fecal streptococci, with the exception of Streptococcus cremoris and Streptococcus mastitidis, act as fermenters of citric acid. The author regards it as especially important that, of twelve different strains of Bacterium coli which were tested, not a single one withdrew carbon from citric acid.

**Changes Caused by Citric Acid Milk in Stools of Nurslings.**—Goeters found that citric acid milk produces a change in the fecal flora of nurslings in that the lactic acid bacilli increase in number, whereas Bacterium coli and the putrefactive bacteria are reduced. The ratio of Bacterium coli to putrefactive bacteria to lactic acid bacteria (Bacterium coli taken as 1) changes from 1:1.3:1.2 to 1:0.5:5.1 mean value. At the same time, feces and urine have a strongly acid reaction.

The stools that are evacuated after feeding with citric acid milk resemble those of breast-fed infants. A few days after the feeding with citric acid milk is changed to feeding with a different formula, the lactic acid bacteria decrease greatly.

## Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4055-4150 (Aug. 20) 1938. Partial Index

*Further Observations on Hypophysio-Endocrine Reactions in Tuberculous Infections. L. Koster and R. de Boer.—p. 4062.
Occurrence of Postvaccinal Encephalitis in Young Children. H. W. Julius.—p. 4071.
Pulmonary Complications During Metrazol Treatment of Patients with Psychoses. A. J. van de Graaff, G. van Montfrans and G. Brouwer. —p. 4078.
Treatment of Addison's Disease. C. L. de Jongh.—p. 4082.

**Hypophysio-Endocrine Reactions in Tuberculous Infections.**—Koster and de Boer in 1935 described a syndrome which occurs in tuberculosis and which is characterized by obesity, erythremia, hypertension, purplish red striae, hyperglycemia, glycosuria, hyperthermia, moderate increase in the cholesterol content of the serum, increase in the basal metabolism and genital anomalies. Because these symptoms are the same as those that have been observed in hypophysial disorders, hypophysial anomalies have been regarded as a causal factor. In the course of the last several years the authors observed additional cases, and in this report they review fourteen in all. They investigated especially the cholesterol ester rate and the lipase content of the serum of these patients. They found that these values are increased in these patients, which is an indication of a hyperfunction of the hypophysis or at least of some of its elements. That this hypophysial disorder is especially frequent in tuberculosis the authors regard as a result of the fact that the immunity reactions of tuberculosis are entirely different from those of other infections. They consider the hypophysial hyperfunction as a form of defense reaction.

## Hospitalstidende, Copenhagen

81: 833-860 (Aug. 30) 1938

*Kraurosis of Vulva. K. E. Christensen.—p. 834.
Retromediastinal Goiter, Diagnosed by Aspiration Biopsy: Case. K. Rohdin.—p. 853.

**Kraurosis of Vulva.**—The first, second and fourth of Christensen's four patients with kraurosis observed in 1937 were over 60 years of age and had had no symptoms of the lesion until fifteen or twenty years after the menopause; the third patient, aged 44, was still menstruating. Hormone analyses made in this case showed no insufficiency. All had had pruritus of the vulva, typical of the lesion, for from three months to seven years, with characteristic gnawing and pricking pain in the vulva, in two instances accompanied by a discharge; in all there were shrinkage of the vulva, leukoplakia and constriction of the introitus. Radical vulvectomy was done in the first three cases and extirpation of the labia in the fourth. The first patient died a year later from complicating cancer, in the next two the symptoms disappeared, and in the fourth they persisted possibly because of the patient's diabetes and the less radical operation. The third patient was given after-treatment with injections of estrogenic substance, in all 80,000 mouse units.

## Norsk Magasin for Lægevidenskapen, Oslo

99: 961-1064 (Sept.) 1938

*Stenosis in Aqueduct of Sylvius from Anatomic Point of View. B. Dahl and F. Harbitz.—p. 961.
*Treatment of Internal Hydrocephalus with Permanent Drainage of Third Ventricle. E. Ingebrigtsen.—p. 976.
Treatment of Gallstones at Naval Hospital from 1919 to 1937. K. Haugseth.—p. 989.
*Observations and Symptoms in Temporal and Occipital Tumors. A. Torkildsen.—p. 996.
Rare Hereditary Anomaly of Pigmentation. H. Sundfør.—p. 1013.

**Stenosis in Aqueduct of Sylvius.**—In the first of Dahl and Harbitz's patients, a man aged 26 with general cerebral symptoms for a year, the diagnosis at necropsy was chronic leptomeningitis, ependymitis granularis and internal hydrocephalus. Examination showed pronounced proliferation of the neuroglia, especially in the third ventricle and about the aqueduct of Sylvius, which was nearly obliterated, a slight inflammation in the choroid plexus and scattered perivascular cell infiltrations about the base of the ventricle system. An inflammation is considered the primary process. In the second patient, a man aged 59 with diffuse cerebral symptoms for three or four years, and marked internal hydrocephalus, an edematous cushion of neuroglia tissue obliterated the aqueduct of Sylvius. There was proliferation of the neuroglia and ependyma, with edema, softening and cystic degeneration. The first, second and third ventricles were dilated. A primary gliomatosis (incipient syringomyelia?) was indicated, especially about the aqueduct of Sylvius, and the atrophy of the medulla oblongata pointed to congenital structural changes as the main cause. In the third patient, a man aged 21 with massive internal hydrocephalus in the first, second and third ventricles for five years, there was ependymitis granularis in the ventricles, with gliomatosis and cystic degeneration around the aqueduct of Sylvius, and stenosis of the aqueduct. In the last patient, a girl aged 14 also with massive internal hydrocephalus, chronic leptomeningo-encephalitis was established, with secondary stenosis of the aqueduct of Sylvius. The hydrocephalus is ascribed partly to the stenosis, partly to the inflammation.

**Internal Hydrocephalus.**—Ingebrigtsen says that internal hydrocephalus is a frequent result of tumors in the third ventricle and of all tumors in the posterior fissure of the brain. In his patient, a man aged 26, a Nélaton catheter No. 8 was introduced through the aqueduct of Sylvius to the third ventricle; its upper end rested in the base of the ventricle, the lower end was passed through the fourth ventricle to the subarachnoid space. The patient became able to work and continued so for more than three years. Four years after the intervention extreme distention of the side ventricles was seen, the tumor in the posterior portion of the third ventricle, originally revealed by ventriculography as a small constant shadow, was now considerably larger, and the inner opening of the drain tube was surrounded by tumor tissue. On puncture of the side ventricles 192 cc. of clear fluid was removed from the right side, 132 cc. from the left side. The patient died in coma. The microscopic diagnosis was ependymoma. The consistency and appearance of the tube were as fresh as on its introduction. The author considers this method of drainage less dangerous than an opening of the base of the third ventricle, which contains the centers for a number of vegetative functions necessary for life. In the second patient, a girl aged 14, a tube was introduced through the aqueduct of Sylvius for permanent drainage of the third ventricle; she died five days later from bronchopneumonia. Immediately after the introduction of the drain tube in the first patient, paralysis of the rectus internus of the right eye occurred which completely receded; in the second case there was somewhat more grave paralysis of the eye muscles.

**Temporal and Occipital Tumors.**—Torkildsen analyzes the seventeen cases of tumor in the temporal lobe and nine of tumor in the occipital lobe of his 154 cases of verified tumors of the brain. The patients were mostly adults; the youngest was 13, the oldest 56. The most important subjective symptoms were, in order, headache, vomiting and, in the patients with occipital tumor, visual disturbances and in those with temporal tumor, focal epilepsy. Mental disturbances in eleven of the first group and seven of the second were seldom noted by the patients with occipital tumor, oftener by those with temporal tumor. All the patients with occipital tumor except one, who was blind, had defects in the visual field, but only two realized the fact. The change first appeared in the lower quadrant. Homonymous hemianopic changes are not recorded in the patients with temporal tumor. Sensory changes were rare. Motor deficiency symptoms were not infrequent in the patients with temporal tumor. Cerebellar dysfunction was frequently present, especially in the patients with occipital tumor. In the patient with aphasia, alexia and apraxia the tumor was mainly in the right hemisphere. Calcium atrophy on the same side as the tumor was established in two cases of temporal tumor, distention of the porus acusticus on the same side as the tumor in one case, and intracerebral calcification corresponding to the site of the tumor in one case. In the cerebrospinal fluid the albumin content was increased; the cell count was not over 16/3.